THE MEDICAL JOURNAL OF AUSTRALIA

VOL. II.—25TH YEAR. SYDNEY, SATURDAY, DECEMBER 31, 1938. No. 27.

Table of Contents

[The Whole of the Literary Matter in THE MEDICAL JOURNAL OF AUSTRALIA is Copyright.]

ORIGINAL ARTICLES— Page.
Sulphanilamide, by BEATRIX DURIE, B.Sc., M.B., Ch.M. .. 1103
The Use of Sulphanilamide in Some Clinical Conditions, by JOHN CHESTERMAN .. 1110
"Q" Fever: Factors Affecting the Appearance of Rickettsiæ in Mice, by F. M. BURNET and M. FREEMAN .. 1114
Observations on Vulvo-Vaginitis in Children, by NORMAN M. GIBSON, O.B.E., M.B., and C. J. WILEY, M.B. .. 1116
Spermatorrhœa in Trichosurus Vulpecula and Other Marsupials, by ADOLPH BOLLIGER and A. L. CARRODUS .. 1118
Blackwater Fever Following the Administration of "Atebrin", by CARL E. M. GUNTHER, M.B., B.S., D.T.M. .. 1119
A Method of Giving Blood Tranfusions to Infants, by V. L. COLLINS, M.D. .. 1121

REPORTS OF CASES—
The Repair of a Facial Nerve Lesion by a Ballance-Duel Graft, by G. A. D. MCARTHUR, M.D. .. 1123

REVIEWS—
Handbook of Practical Bacteriology .. 1124
Tropical Nutrition and Dietetics .. 1124

LEADING ARTICLES—
New Year's Eve .. 1125

CURRENT COMMENT—
Accessory Spleens .. 1126

BRITISH MEDICAL ASSOCIATION NEWS—
Scientific .. 1127
Annual Golf Competition Conducted by the New South Wales Branch .. 1129
Nominations and Elections .. 1129

MEDICAL SOCIETIES— Page.
Melbourne Pædiatric Society .. 1129

MEDICAL PRACTICE—
Report of the Committee Appointed to Observe the Kenny Method of Treatment for Paralysis at London .. 1133

THE ROYAL AUSTRALASIAN COLLEGE OF PHYSICIANS—
Inaugural Ceremony .. 1137
Examination for Membership .. 1141

OBITUARY—
Harrie Carisfort Edmond Donovan .. 1142
James Cook .. 1143
Keith Moore Whiting .. 1143
Archibald Brown Campbell .. 1143

CORRESPONDENCE—
The First Fifty-two Names in the Medical Register of South Australia .. 1143
Accidental Hæmorrhage .. 1143

NOTICE .. 1143

BOOKS RECEIVED .. 1143

DIARY FOR THE MONTH .. 1144

MEDICAL APPOINTMENTS VACANT, ETC. .. 1144

MEDICAL APPOINTMENTS: IMPORTANT NOTICE 1144

EDITORIAL NOTICES .. 1144

SULPHANILAMIDE.[1]

By BEATRIX DURIE, B.Sc., M.B., Ch.M.,
Sydney.

SULPHANILAMIDE is the name first used by Fuller[(1)] and adopted by the Council on Pharmacy and Chemistry of the American Medical Association[(2)] as a convenient abbreviation for p-amino benzene sulphonamide. This substance has been shown by English and American workers to be the active portion of the molecule of "Prontosil", a drug which was first introduced to the medical profession by Domagk[(3)] in February, 1935. "Prontosil" was received with immediate enthusiasm, not only by the medical profession, but by scientific workers generally and by the great manufacturing drug houses. Three years ago it would have been a comparatively easy task to describe what was known of "Prontosil" and its effect on hæmolytic streptococcal infections. Today this new chemotherapy is an extremely difficult subject about which to speak, for the introduction of one drug has led to the study of many hundreds of related compounds, and the effective scope of the action of all these substances has widened to include infections produced by several different organisms. In a short paper such as this it is impossible to do more than give the barest outline of the work that has been done. Several excellent reviews of the subject have recently appeared in English and American journals,[(4)(5)(6)(7)(8)] and those who have read these will not, I am afraid, find much that is new in what I have to say.

[1] Read at a meeting of the New South Wales Branch of the British Medical Association on October 27, 1938.

History.

To appreciate the work which led to the discovery of "Prontosil" we must go quite a long way back into the history of organic chemistry. Most medical practitioners are familiar with the formula of azo-benzene, first synthesized in 1860, and you know that a number of compounds derived from azo-benzene and its homologues have been used as dyes in the textile industry for the past twenty-five years. Some of these dyes are believed to form a chemical combination with the protein of the wool fibre. It was this property of azo-dye substances which suggested their use as antiseptics and chemotherapeutic agents; it was hoped that they might form chemical combinations, analogous to those formed in dyeing fabrics, with the protein of the bacterial or protozoal cell. Ehrlich and his school believed in chemical specificity as the essential feature of the antigen-antibody reactions; and one can easily see how this belief led to the search for specific chemotherapeutic agents. It seemed to be easier to attack the more highly developed organisms; the best results were obtained in spirochætal and in protozoal disease. The search for a chemical substance which would be effective in bacterial infections has been, until recently, very disappointing. The chemists succeeded in finding a group of highly efficient disinfectants, but not a single product which could be used for the destruction of bacteria in the living body.

In 1913 Eisenberg tested the action of one of the azo-dyes, chrysoidin, on bacteria *in vitro*, and found that it had a strong bactericidal effect, but that this effect could not be reproduced in the living animal. Various other compounds, trypan red, trypan blue, the acridine compounds, and so on, were tested in this way, particularly as urinary antiseptics, but with unsatisfactory therapeutic results. Actually, Eisenberg came fairly close to discovering "Prontosil" in 1913, for the first compound known by that name, patented nineteen years later, in 1932, by Mietsch and Klarer, was the hydrochloride of sulphamido-chrysoidin. New as a therapeutic agent, it was not new as a dye: for, according to Hörlein[9] similar azo-dyes with sulphonamide and substituted sulphonamide groups had been used for some years. The addition of the sulphonamide group improved the fastness of the dye. The observation of Domagk of the action of one of these dyes on streptococci turned the experimental elaboration of fast dyes into something far more exciting and led to what is perhaps the greatest chemotherapeutic advance of the century. "Numerous *new* azo-dyes containing sulphonamide were prepared", writes Hörlein,[9] "but the test object was no longer the wool-fibre, it was the mouse infected with hæmolytic streptococci."

It was Marco Polo who described a race of people "who went about making discoveries by accident and sagacity, of things they were not in search of". This phrase might describe the scientists whose search for new dyes led to the discovery of a chemotherapeutic agent; but we must emphasize the sagacity more than the accident, for "chance favours the prepared mind", and the minds of the dye chemists had been prepared for a great chemotherapeutic discovery ever since the time of Ehrlich. An immense amount of "blind, laborious work", in the course of which (to quote Hörlein[9]), "the sphere of the azo-dye stuffs as well as many other substances had been thoroughly investigated", had preceded the discovery; and I should like to follow Professor Garrod[4] in emphasizing that the credit of making the greatest discovery in modern therapeutics belongs entirely to the staff of the Institute of Experimental Pathology and Bacteriology of the I. G. Farbenindustrie, Elberfeld. The discovery of sulphanilamide, suggested by French workers and completed by English and American workers, was only a secondary discovery. It was the German workers who blazed the trail.

It was evident from the beginning that there was something new about the way "Prontosil" acted. The antiseptic qualities of chrysoidin had been reduced by the addition of the sulphonamide group, but the therapeutic action *in vivo* was actually increased. When one-tenth to one-fiftieth of the maximum tolerated dose of this drug was given to mice after intraperitoneal injection of fatal doses of hæmolytic streptococci, the mice did not die.

Unfortunately, the name "Prontosil" has been given to at least three different compounds. The first of these, for which Mietsch and Klarer obtained a patent on Christmas Day, 1932, was the hydrochloride of sulphamido-chrysoidin (4′-sulphamido-2-4-diamino-azo-benzene), a red crystalline powder slightly soluble in water. The second "Prontosil" was the dihydrochloride of sulphamido-chrysoidin, slightly more soluble in water and just as effective, known as "Prontosil Flavum", patented in France as "Rubiazol". The third "Prontosil" was the di-sodium salt of 4′-sulphamido-2-azo-1-hydroxy-7-acetylamino-naphthalene-3-6-disulphonic acid. Known as "Prontosil" or "Prontosil Soluble", this substance, a red dyestuff, was at first sold in 2·5% solution; it is now sold in 5% solution and is also now put up for sale for oral administration, under the title of "Neo-prontosil".

These three substances had very little effect on hæmolytic streptococci *in vitro*. The German workers had not furnished an explanation of their efficacy *in vivo*; they were presented to the world as an "astonishingly efficient mystery", to use Garrod's[9] phrase, and a mystery they remained until later in the same year (1935), when Tréfouël, Tréfouël, Nitti and Bovet[10] put forward the hypothesis that activity resided in that part of the molecule which consisted of a sulphonamide group attached to one benzene nucleus. They tested the therapeutic activity of this simpler compound and found it equal to that of "Prontosil" itself. Further studies by other French workers, by Buttle *et alii*,[11][12] by Fuller,[1] and by Bliss and Long[12] established the correctness of this discovery. Here, then, was a surprise. Work on the azo-dyes, pursued for so many years, had led to the discovery of a simple, colourless, therapeutic agent, which was not

a dye at all. This relatively simple compound was not even new, having been synthesized fully thirty years before. Its antibacterial action, by the way, had just missed discovery in 1919 by workers at the Rockefeller Institute, New York. In that year Heidelberger and Jacobs had reported that a group of substances including the m- and p-aminobenzene-sulphonamides appeared to have considerable antibacterial activity and that this problem would be discussed by Dr. Martha Wollstein. There is, however, no further mention of Martha Wollstein's work in the literature.

The name "p-amino-benzene-sulphonamide" was first abbreviated to "sulphonamide"; but this was hardly distinctive enough, and, as we have seen, the name "sulphanilamide" was adopted and came into general use. Domagk still maintains that "Prontosil" is superior to sulphanilamide and that the azo-dye linkage is important; but the weight of evidence is against this view. Sulphanilamide is marketed under the various names of "Prontosil Album", "Prontylin", "Stramid", "Streptocide", "Sulphonamide-p" *et cetera*. The term "Prontosil" should be reserved for the earlier compound, the di-hydrochloride of sulphamido-chrysoidin; while the naphthalene compound is usually known as "Prontosil Soluble". The nomenclature of these drugs has been, and still is, most confusing.

Clinical Results.

"Prontosil", "Prontosil Soluble" and sulphanilamide have now been used successfully in the treatment of infections due to the following organisms: *Streptococcus hæmolyticus* (groups *A* and *C*),[13] meningococcus, gonococcus, pneumococcus (Type III), *Clostridium welchii*,[13] and *Plasmodium malariæ*.[14]

Sulphanilamide is believed to be of some use in the treatment of infections due to *Brucella abortus*,[15][16] *Brucella melitensis*,[15][16] *Bacillus typhosus*,[17] and is of doubtful value in infections due to *Streptococcus hæmolyticus* (groups *B*, *E* and *G*).[18]

The literature contains accounts of its use in other miscellaneous conditions; but the evidence of its use in these as yet is inadequate.

Urinary infections come in a category by themselves, because the concentration of sulphanilamide attainable in the urine is much higher than concentrations found in other parts of the human body. It has been used with success in urinary infections[19][20] due to *Bacillus coli*, *Bacillus lactis aerogenes*, *Bacillus proteus*, *Pseudomonas pyocyanea*, *Staphylococcus aureus*, as well as urinary infections with the organisms mentioned in the two previous lists.

It is apparently of no value in infections due to *Streptococcus hæmolyticus* (group *L*),[18] *Streptococcus viridans* or anaerobic streptococci, in rheumatic fever[21] or in experimental syphilis. (I have purposely mentioned infecting organisms, not clinical conditions, because it needs to be emphasized that sulphanilamide is simply one method of attacking the infecting organism; it does not supplant surgical and other methods of treatment when these are indicated.)

Infection with Streptococcus Hæmolyticus.

Of the hæmolytic streptococcal infections in which it has been used, good results have been obtained in erysipelas, *otitis media*, meningitis, puerperal fever, pneumonia, empyema, burns and cellulitis. On the other hand, in acute and chronic tonsillitis, sinus infections, scarlet fever and osteomyelitis the results are not remarkable.

"Prontosil" and, later, sulphanilamide were at first used quite empirically in the treatment of these conditions. Let us see if some explanation of the various effects produced can be found in what is known of the pharmacology of the drug.

Pharmacology.

Sulphanilamide is a white, crystalline powder, readily soluble in hot water, sparingly soluble in cold (0·8%). It is relatively inexpensive. The best pharmacological study hitherto published is found in the work of Marshall, Emerson and Cutting,[23][24] of the Johns Hopkins Hospital. Marshall[22] has evolved a simple method of estimating the amount of sulphanilamide present in the blood, urine and other body fluids. To quote their description: "This method is based on diazotization of the sulphanilamide with nitrous acid and the coupling of the resulting diazo compound in acid solution with dimethyl-α-naphthylamine to produce a purplish-red azo-dye which can easily be estimated by colorimetric comparison. This reaction depends on the presence of an amine group substituted in the benzene ring, and serves to estimate any compound to which the sulphonamide is changed in the organism and in which the amine group is intact. This colour reaction is exceedingly delicate, being detectable in a solution of one part of sulphanilamide in twenty million parts of water." For blood the procedure is somewhat the same, the test being performed on a protein-free filtrate of the blood, which is best prepared by using saponin and p-toluene-sulphonic acid. We have used these methods at the Women's Hospital, Crown Street, The tests are very simple ones; the only difficulty is to procure satisfactory supplies of di-methyl-α-naphthylamine and p-toluene-sulphonic acid. The colour of the unknown is sometimes very slightly different from that of the standard; this seems to be a matter of adjusting the reaction of the urine or of the blood filtrate. Many other substances besides di-methyl-α-naphthylamine will give a useful colour reaction. Dobbs and Geiger[38] have tried several other substances for the coupling reaction; they recommend di-phenylamine.

Absorption.

Armed with these methods of analysis, Marshall, Cutting and Emerson[23][24] have demonstrated by repeated blood estimations the following facts about the absorption of sulphanilamide.

1. It is rapidly absorbed from the gastro-intestinal tract—as easily absorbed as alcohol.
2. It reaches the peak of concentration in the blood in about three hours.
3. The absorption is complete in about four hours.
4. It enters the circulation at the same rate if given by mouth as if given subcutaneously.

There is no advantage in parenteral injection unless the patient is vomiting. The persistence in the blood is important. Garrod[4] comments that other chemotherapeutic agents have failed because they are so rapidly eliminated that an adequate blood level is not maintained. Marshall[18] and his colleagues claim to have shown that this persistence in the blood is due to the reabsorption in the renal tubules of 70% to 80% of the sulphanilamide in the glomerular filtrate. Concentrations recorded in the blood in human beings vary from 4·0 to 25·0 milligrammes per hundred cubic centimetres. According to Bliss and Long[26] the optimum concentration in the blood, in hæmolytic streptococcal infections, is 10·0 milligrammes per hundred cubic centimetres. Dr. Chesterman will discuss the dosage necessary to maintain this.

Distribution in the Body.

Once sulphanilamide has entered the blood stream it is distributed to all parts of the body, like alcohol and urea. It resembles urea in its approximately even distribution in the water of the body. After oral administration it has been found in the blood and in pleural and peritoneal effusions, in saliva, in pancreatic juice, in bile, in the cervical secretion, in amniotic fluid, in the tears and in the cerebro-spinal fluid. It is present in breast milk in higher concentration than in the blood. There is some difference of opinion as to whether infants should be breast fed by a mother to whom large doses of sulphanilamide are being given.

In the cerebro-spinal fluid the curve of concentration parallels that of the blood at about three-quarters of the blood level.[23] Marshall, Emerson and Cutting[25] emphasize the fact that no difference appears to exist in the passage of sulphanilamide into the spinal fluid of normal human beings and in those suffering from meningococcal meningitis. This fact establishes the value of sulphanilamide when given by mouth in the treatment of bacterial meningitis. Whether combined intrathecal therapy is necessary or not must be decided by clinical study. Sulphanilamide is superior in this respect to "Prontosil Soluble", which passes very slowly from blood to cerebro-spinal fluid and which is dangerous if injected intrathecally.

Skeletal muscle, heart muscle, liver, lung and spleen[24] contain approximately the same concentration as blood, skin containing slightly less; brain contains about two-thirds the concentration present in blood, and bone and fat contain the drug in a much lower concentration than blood.[24] This latter fact may have some bearing on the observation that the results of treatment by sulphanilamide of hæmolytic streptococcal osteomyelitis are not remarkable.

Excretion.

Sulphanilamide is almost wholly excreted in the urine, where it appears in both free and conjugated forms.[1][23] It appears in the urine fifteen minutes after intramuscular injection. Excretion is complete in two or three days, and is delayed when the kidneys are damaged.[23][24] Much higher concentrations are attainable in urine than in blood, concentrations as high as 125 milligrammes per 100 cubic centimetres having been recorded.[26] Concentrations of 40 to 50 milligrammes per 100 cubic centimetres are quite easily maintained. We have observed such concentrations in patients treated with small doses at the Women's Hospital, Crown Street. Sulphanilamide tends to produce an acidosis, associated with the excretion of an alkaline urine containing large amounts of sodium. Sodium bicarbonate should be given to prevent this acidosis. Rimington[27] has recently observed that increased excretion of porphyrins in the urine occurs when patients and rats are given sulphanilamide.

Mode of Action.

The original animal experiments[3][28] showed that when "Prontosil" was administered to mice immediately after experimental infection with hæmolytic streptococci it exerted a protective action which lasted as long as its administration was continued. But if the administration of the drug was delayed for several hours after the mice had been inoculated with hæmolytic streptococci, or if the treatment was stopped before the animal had recovered, the streptococci revived, the infection gained the upper hand, and the mice died. This suggests that "Prontosil" affects the hæmolytic streptococcus in some way, or arrests its multiplication in the body.

Sulphanilamide has a demonstrable effect on bacteria outside the body. Bliss and Long[29] described the first detailed experiments illustrating the effect of sulphanilamide on hæmolytic streptococci *in vitro*. "A concentration of no more than one part in 18,000 prevented the growth of small numbers of streptococci (a few hundreds or perhaps thousands per cubic centimetre), but not the millions introduced by an inoculum of undiluted culture."[4] Concentrations of 1 in 10,000 are definitely bacteriostatic, and, as we have seen, concentrations of 1 in 10,000 are attainable in the blood stream. In their earlier work Bliss and Long[29] suggested that in addition to this bacteriostatic effect, sulphanilamide damaged the streptococci in some way and made them more susceptible to phagocytosis.

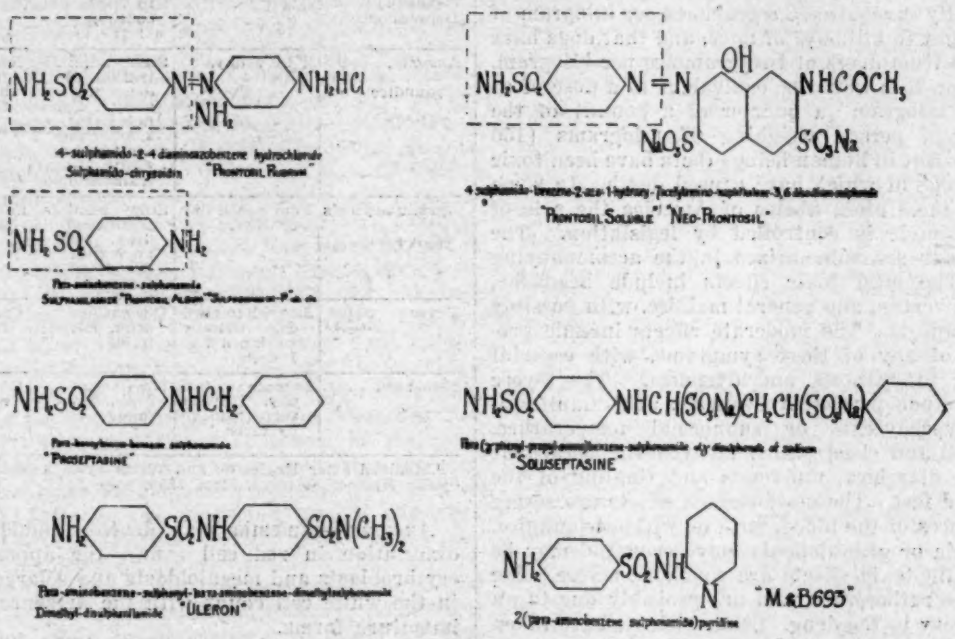
It must be remembered that a healthy animal or a healthy human being is well able to cope with small numbers of hæmolytic streptococci. Hæmolytic streptococcal infections—scarlet fever, tonsillitis, mild puerperal infections without septicæmia—tend towards recovery without any specific treatment. It is only when the infection is a severe one, when the natural resistance is overwhelmed, and the streptococci have it all their own way and multiply rapidly in the peritoneal cavity or in the blood stream, that

life is threatened. One reason for this tendency to recovery in mild infections is that the phagocytes of the blood stream can deal with a few hæmolytic streptococci at a time. The infection itself, without any drug, stimulates the resistance of the body to a certain extent. The appearance of a leucocytosis is one evidence of this. Tillett[31] has recently shown that sera obtained from patients at the time of acute active infection with various organisms were in every instance bactericidal to hæmolytic streptococci. In some of these patients a leucocytosis was present, in others a leucopenia; this did not affect the bactericidal effect of the serum. It is obvious that these facts are of great importance in assessing the value of *in vivo* and *in vitro* experiments with sulphanilamide. When defibrinated blood or serum is mixed with a chemical any antibacterial power of the mixture is a summation of the antibacterial power of the blood and of the chemical. This fact, and the circumstance that some workers have used very heavy inocula of bacteria, make it difficult to assess the value of experiments testing the effect of blood or serum, with added sulphanilamide, on hæmolytic streptococci *in vitro*.

The consensus of opinion at present seems to be that sulphanilamide acts simply by slowing down or preventing the multiplication of the infecting organism and giving the natural powers of resistance a chance. Longcope[8] writes:

> Further work by Long and Bliss[30] and by Gay and Clark[32] seems to show that the drug simply retards the growth of hæmolytic streptococci in the peritoneum of the mouse or in the pleural cavity of rabbits and that it has *in vivo* no other demonstrable property than that which it possesses *in vitro*, namely one of bacteriostasis . . . The actual cure of the infection and the elimination of the hæmolytic streptococci depends in the last analysis not upon the drug but upon the protective forces of the body.

That neutrophile cells are essential to the protective action of sulphanilamide in the mouse is indicated rather neatly by the experiments of Long and Bliss,[30] who found that treatment by sulphanilamide became completely ineffective in mice made leucopenic by injections of benzene. These workers have shown that bacteriostasis is the only demonstrable factor in the process which leads to the control of *Clostridium welchii* infection in mice treated with sulphanilamide.



Bacteriostasis in the case of a severe hæmolytic streptococcal infection means a great deal. It means the arrest of the production of toxins, of the production of hæmolysin and of leucocidin; so that the drug may appear to enhance the powers of resistance of the body, when it is really only checking the powers of the invading organism. There is no proof that sulphanilamide alters the virulence of the infecting organism, or that it affects capsule production or that it has any remote and mysterious effects on the reticulo-endothelial system. It is of interest to note that recent observations show that in meningococcal and in pneumococcal infections its action is increased by the giving of immune serum.

Local treatment by "Prontosil" has not been successful; sulphanilamide should theoretically be of more use. Purdie and Fry[33] have successfully used a combination of local and general treatment on two patients with persistent sinuses infected with hæmolytic streptococci. There is no record of a series of wounds treated by sulphanilamide; one

would expect it to be of most use in deep wounds where it could be retained and where the tissue fluids could participate in the healing. Most observers agree that neither local nor general treatment is of any use in chronic throat infections or in carrier states.

Toxic Effects.

When first discovered, sulphanilamide was thought to be almost innocuous, for its toxic effects were not foreshadowed by animal experiments. Except in enormous doses, it is almost harmless to laboratory animals. Marshall, Cutting and Emerson[34] found that when the drug was administered orally it required 3·8 grammes per kilogram of body weight to kill 50% of mice, and that dogs have recovered from doses of two grammes per kilogram. This latter dose would be equivalent to a dose of at least 0·1 kilogram (a quarter of a pound) of the drug for a person weighing 67 kilograms (150 pounds). But in human beings there have been toxic effects, some of which have caused death. In some parts of the United States of America the sale of sulphanilamide is controlled by legislation. The toxic effects are summarized in the accompanying table. The mild toxic effects include headache, anorexia, vertigo and general malaise, with possibly slight cyanosis. The moderate effects include progression of any of these symptoms, with especial reference to cyanosis and dyspnœa. The severe effects include persistent cyanosis, skin manifestations, hyperpyrexia or subnormal temperature, abdominal and chest pains, tachycardia, persistent dyspnœa, diarrhœa, numbness and tingling of the hands and feet. The most serious effects are severe disturbances of the blood, with or without jaundice. Leucopenia or granulopenia may occur and may be fatal. Mild toxic effects are common; severe toxic effects are rather rare, and are probably due to an idiosyncrasy to the drug. Some patients have taken 1·2 to 2·4 grammes of the drug daily for months without any ill effects, but in other cases severe cyanosis or anæmia has followed small doses. Fatal agranulocytosis has not been reported before the fourteenth day of treatment.

Cyanosis.—Some degree of cyanosis occurs in 75% of patients. Authorities differ as to the cause of this. In severe cyanosis the blood has been found to contain large quantities of sulphæmoglobin or methæmoglobin or, more rarely, of both. We have seen instances of this at the Women's Hospital.

In 1936 a nurse suffering from sore throat took a small dose of "Prontosil", some phenacetin and an aperient. Next day she was deeply cyanosed; her face was literally dark blue. She had severe dyspnœa. The blood contained both sulphæmoglobin and methæmoglobin, and it was at least six weeks before this girl's colour was normal.

Marshall and Walzl,[35] who record the presence of cyanosis when neither methæmoglobin nor sulphæmoglobin could be detected in the blood, have postulated the existence of a peculiar erythrocyte-binding pigment in the blood. However, they have been unable to isolate such a pigment.

TABLE I.[1]

Toxic Manifestations of Sulphanilamide.

Symptoms and Signs.	Time of Appearance.	Treatment.	Outcome.
Cyanosis (slight)	First or second 24 hours	None, unless dyspnœa is present	Recovery is prompt
Cyanosis (severe)	First or second 24 hours	Discontinue drug; give fluids in large quantities	Recovery
Nausea Vomiting Giddiness Weakness Headache Depression	First 24 hours or longer	None. These symptoms are not usually severe enough to cause discontinuance of the drug	
Anæmia, with or without jaundice	2 to 7 days	Stop administration of drug immediately. Force fluids to 3,000 cubic centimetres daily. Blood transfusion	Recovery from blood transfusion
Agranulocytosis	Fourteenth day or later	Stop administration of drug. Pentnucleotide. Blood transfusion	Fatal in most cases
Fever	Seventh to ninth day. Usually continues 2 to 6 days	Discontinue drug. Force fluids	Complete recovery
Skin rash	Seventh to ninth day. Usually accompanied by fever	Discontinue drug. Force fluids	Complete recovery

[1] Modified after Eggleston and Weiss (*The American Journal of the Medical Sciences*, May, 1938, page 701).

Anæmia.—Anæmia may develop suddenly, with diminution in red cell count, the appearance of erythroblasts and megaloblasts and a large increase in the white cell count with the presence of many immature forms.

Agranulocytosis.—It is not surprising that agranulocytosis should occur, as it has been known for some time that drugs possessing in common a benzene ring with an attached amine group may cause agranulocytosis in susceptible individuals. Leucocyte counts should be performed at frequent intervals on patients receiving the drug, though frequent white blood cell counts gave no warning of impending disaster in the case reported by Young.[36]

Hyperpyrexia.—Hyperpyrexia may be rather troublesome, as it may be difficult to know whether it is due to the drug or to the disease. Garrod[4] has suggested that the fever may be a reaction to the products of lysed bacteria.

Skin Manifestations.—Various types of rashes have been described—morbilliform, scarlatiniform and urticarial. Exfoliative dermatitis may occur. Rashes are most common on the parts of the body exposed to sunlight, and are seen more frequently in ambulatory patients. Rimington's[37] observations on the excessive urinary excretion of porphyrins

have led him to suggest that photosensitization is the cause of these skin manifestations.

Optic Neuritis.—A rare but alarming toxic symptom is optic neuritis.[37]

Remote Effects.—These are all more or less immediate results of sulphanilamide treatment. Whether any remote effects will appear remains for the future to disclose.

Further Investigation.

So far, sulphanilamide is the only one of the large series of compounds related to "Prontosil" which has been fully investigated experimentally. An immense amount of work remains to be done. Of the compounds which have received clinical trial I may mention "Uleron" (di-methyl-di-sulphanilamide), "Proseptasine" (p-benzyl-amino-benzene-sulphonamide), "Soluseptasine" or p(γ phenyl-propyl-amino) benzene-sulphonamide-αγ-disulphonate of sodium, and "M and B 693", 2(p-amino benzene-sulphonamido)pyridine, which appears to have a remarkable effect on most pneumococcal infections, and also on hæmolytic streptococcal and meningococcal infections. Even these few drugs cannot be grouped together indiscriminately; for instance, the treatment of gonorrhœa with "Uleron" has been followed by peripheral neuritis, which has not occurred after the use of any other drug in this series, and "Proseptasine" has no effect on meningococcal infections. These individual differences make it advisable to use sulphanilamide whenever possible; at least until more is known of the other drugs. In time we may hope to possess a series of drugs at least as efficacious in the treatment of bacterial infections as those now used in the treatment of protozoal disease. Even the virus diseases may be conquered by the remarkable work of present-day chemists; for Dochez[8] has recently found that sodium sulphanilyl sulphanilate has a remarkably beneficial effect in distemper. I think we may confidently expect further discoveries of great importance. It will be extraordinarily interesting to follow the development of this work during the next few years.

References.

(1) A. Fuller: "Is Sulphanilamide the Active Agent in 'Prontosil' Therapy?" *The Lancet*, Volume I, January 23, 1937, page 194.

(2) Report of the Council on Pharmacy and Chemistry of the American Medical Association: "Sulphanilamide and Related Compounds", *The Journal of the American Medical Association*, Volume CVIII, May 29, 1937, page 1888.

(3) G. Domagk: *"Ein Beitrag zur Chemotherapie von Bakterieller Infectionen"*, *Deutsche medizinische Wochenschrift*, Volume LXI, February 15, 1935, page 250.

(4) L. P. Garrod: "The Chemotherapy of Bacterial Infection", *The Lancet*, May 14 and 21, Volume I, 1938, pages 1125, 1178.

(5) M. A. Schnitker: "Sulphanilamide: A Review", *The New England Journal of Medicine*, Volume CCXVIII, March 24, 1938, page 503.

(6) W. L. Holman and G. L. Duff: "Sulphanilamide and Similar Compounds in Chemotherapy", *The American Journal of the Medical Sciences*, Volume CXCV, March, 1938, page 379.

(7) C. Eggleston and S. Weiss: "The Use of Sulphanilamide in the Treatment of Various Infections", *The American Journal of the Medical Sciences*, Volume CXCV, May, 1938, page 701.

(8) W. T. Longcope: "Problems Relating to the Invasive Properties of Hæmolytic Streptococci and their Control by Sulphanilamide", *The American Journal of the Medical Sciences*, Volume CXCV, May, 1938, page 577.

(9) H. Hörlein: "The Chemotherapy of Infectious Diseases caused by Protozoa and Bacteria", *Proceedings of the Royal Society of Medicine*, Volume XXIX, April, 1936, page 314.

(10) J. Tréfouël, Madame J. Tréfouël, F. Nitti and D. Bovet: *"Activité du p-aminophénylsulfamide sur les infections streptococciques expérimentales de la souris et du lapin"*, *Comptes rendus des séances de la Société de biologie*, Volume CXX, 1935, page 756.

(11) G. A. H. Buttle, H. J. Parish, M. McLeod and D. Stephenson: "The Chemotherapy of Typhoid and Some Other Non-Streptococcal Infections in Mice", *The Lancet*, Volume II, March 26, 1937, page 681.

(12) E. A. Bliss and P. H. Long: "Activation of 'Prontosil Solution' in Vitro by Reduction with Cysteine Hydrochloride", *Bulletin of the Johns Hopkins Hospital*, Volume LX, 1937, page 149.

(13) S. R. Bohlman: "Gas Gangrene Treated with Sulphanilamide: Report of Three Cases", *The Journal of the American Medical Association*, Volume CIX, July 24, 1937, page 254.

(14) R. A. Hill and M. H. Goodwin: "'Prontosil' in Treatment of Malaria: Report of 100 Cases", *The Southern Medical Journal*, Volume XXX, 1937, page 1170 (quoted by Garrod[4]).

(15) A. L. Punch: "Undulant Fever Treated with Prontosil", *The Lancet*, Volume II, August 20, 1938, page 429.

(16) R. Stern and K. W. Blake: "Undulant Fever and its Treatment with Sulphanilamide", *The Journal of the American Medical Association*, Volume CX, May 7, 1938, page 1550.

(17) M. Barer: "Typhoid Bacilluria Treated by Sulphanilamide", *The Lancet*, Volume II, October 23, 1937, page 964.

(18) E. A. Bliss and P. H. Long: "Failure of p-aminobenzene-sulphonamide Therapy in Urinary Infections due to Group D β-Hæmolytic Streptococci", *The New England Journal of Medicine*, Volume CCXVII, 1937, page 81 (quoted by Garrod[4]).

(19) H. F. Helmholz: "The Bactericidal Power of the Urine after the Administration of Prontosil by Mouth", *Proceedings of the Staff Meetings of the Mayo Clinic*, Volume XII, April 21, 1937, page 244.

(20) H. F. Helmholz and A. E. Osterberg: "Rate of Excretion and Bactericidal Power of Sulphanilamide in the Urine", *Proceedings of the Staff Meetings of the Mayo Clinic*, Volume XII, June 16, 1937, page 377.

(21) H. F. Swift *et alii*: "The Action of Sulphanilamide in Rheumatic Fever", *The Journal of the American Medical Association*, Volume CX, February 5, 1938, page 426.

(22) E. K. Marshall, junior: "The Determination of Sulphanilamide in Blood and Urine", *The Journal of Biological Chemistry*, Volume CXXII, December, 1937, page 263.

(23) E. K. Marshall, junior, K. Emerson and W. C. Cutting: "Para-amino-benzene-sulphonamide", *The Journal of the American Medical Association*, Volume CVIII, March 20, 1937, page 953.

(24) E. K. Marshall, junior, W. C. Cutting and K. Emerson: "The Distribution of Sulphanilamide in the Organism", *The Journal of Pharmacology and Experimental Therapy*, Volume LXI, 1937, page 196.

(25) E. K. Marshall, junior, and W. C. Cutting: "Sulphanilamide in Bacterial Meningitis", *The Lancet*, May 21, 1938, page 1186.

(26) D. R. Mitchell: "A Preliminary Report on Sulphanilamide as a Urinary Antiseptic", *The Canadian Medical Association Journal*, July, 1938, page 22.

(27) C. Rimington and A. W. Hemmings: "Porphyrinuria following Sulphanilamide", *The Lancet*, April 2, 1938, page 770.

(28) L. Colebrook and M. Kenny: "The Treatment of Human Puerperal Infections and of Experimental Infection in Mice with Prontosil", *The Lancet*, Volume I, June 6, 1936, page 1279.

(29) P. H. Long and E. A. Bliss: "Para-amino-benzene-sulphonamide and its Derivatives", *The Journal of the American Medical Association*, Volume CVIII, January 2, 1937, page 32.

(30) E. A. Bliss and P. H. Long: "The Mode of Action of Sulphanilamide", *The Journal of the American Medical Association*, Volume CIX, November 6, 1937, page 1524.

(31) W. S. Tillett: "The Bactericidal Action of Human Serum on Hæmolytic Streptococci", *The Journal of Experimental Medicine*, Volume LXV, January, 1937, page 147.

(32) F. P. Gay and A. R. Clark: "On the Mode of Action of Sulphanilamide in Experimental Streptococcal Empyema", *The Journal of Experimental Medicine*, Volume LXVI, 1937, page 535.

(33) A. W. Purdie and R. M. Fry: "Chronic Hæmolytic Streptococcal Infection Treated with p-amino Benzene Sulphonamide", *The Lancet*, Volume II, July 3, 1937, page 18.

(34) E. K. Marshall, junior, W. C. Cutting and K. Emerson: "The Toxicity of Sulphanilamide", *The Journal of the American Medical Association*, Volume CX, January 22, 1938, page 252.

(35) E. K. Marshall, junior, and E. M. Walzl: "On the Cyanosis from Sulphanilamide", *Bulletin of the Johns Hopkins Hospital*, Volume LXI, August, 1937, page 140.

(36) C. J. Young: "Agranulocytosis and Sulphanilamide", *The British Medical Journal*, Volume II, July 17, 1937, page 105.

(37) P. C. Bucy: "Toxic Optic Neuritis Resulting from Sulphanilamide", *The Journal of the American Medical Association*, Volume CIX, September 25, 1937, page 1007.

(38) J. Dobbs and J. C. Geiger: "The Determination of Sulphanilamide in Urine and Blood", *The Journal of Laboratory and Clinical Medicine*, Volume XXIII, March, 1938, page 651.

THE USE OF SULPHANILAMIDE IN SOME CLINICAL CONDITIONS.[1]

By JOHN CHESTERMAN,
Sydney.

SINCE the introduction of sulphanilamide three years ago, the literature on the subject has grown steadily, and merely to read a list of articles published in the English medical literature alone, would in itself take up most of the time at my disposal. Dr. Durie in her paper has tabulated the organisms against which sulphanilamide compounds are known to be active in some degree, and it is obviously impossible in a short time to deal adequately with its use and value in the numerous clinical diseases that these organisms produce. Hence my remarks will be confined to conditions in which I have had the opportunity of employing it; but I hope that in discussion other speakers will refer to its indications and value in conditions such as gonorrhœa and the pneumonias.

I shall deal first with infections following childbirth or abortion. Since a number of organisms are responsible for these genital tract infections, it follows that rational treatment rests essentially on bacteriological diagnosis. The indiscriminate administration of sulphanilamide for fever following abortion or in the puerperium is unjustified, because of the possible toxic effects. Moderate doses may in some instances be given while a bacteriological report is awaited; but they should be stopped unless the report indicates continuance.

The organisms concerned in the more severe forms of puerperal infection are the following:

1. Hæmolytic streptococci (Lancefield's group *A*). Hæmolytic streptococci belonging to groups *B*, *C* and *D* are occasionally associated with infection, but these infections are seldom severe.
2. Anaerobic streptococci.
3. Other streptococci, such as *Streptococcus viridans* and aerobic non-hæmolytic streptococci.
4. The *Bacillus coli* group.
5. *Clostridium welchii* and other spore-bearing anaerobic organisms.
6. Staphylococci.
7. Non-specific organisms, recovered in many less severe puerperal infections.

Fortunately it is against the hæmolytic streptococci that sulphanilamide has its most dramatic and decided effect. In the past the group *A* hæmolytic streptococci have been responsible for about 70% of the deaths following puerperal infection. There is now ample experimental and clinical evidence of the effect of sulphanilamide, and there is statistical evidence from various parts of the world that indicate a reduction in mortality rates concurrent with its introduction and use. For instance, in New South Wales in 1937 the maternal mortality rate from puerperal sepsis was reduced by 28% in comparison with the average rate of the previous five years. To what extent this improvement may be due to a diminished virulence of the hæmolytic streptococci only time can show. During the past two years 75 patients with β hæmolytic streptococcal infections originating in the genital tract have been treated with sulphanilamide or related compounds at the Women's Hospital, Crown Street, Sydney; and through the kindness of my colleagues I have had an opportunity of observing most of them. The results are set out briefly in Table I.

[1] Read at a meeting of the New South Wales Branch of the British Medical Association on October 27, 1938.

TABLE I.

Genital Tract Infections by β-Hæmolytic Streptococci Treated by Sulphanilamide or Related Compounds.

Severity of Infection.	Extent of Infection.	Number of Patients.	Deaths.[1]
Grade I	Local uterine infections	58	0
Grade II	Beyond the uterus, but limited to the pelvis	9	0
Grade III	Beyond the pelvis (that is, septicæmia or peritonitis, or both)	8	4
	Total	75	4

Mortality rate = 5·3%.

[1] Three of the four patients who died had already severe infections before admission to hospital.

Unfortunately there is no control series for comparison; but I can say with certainty that the number of deaths from sepsis in the hospital from all causes during this period has fallen by more than one-half in comparison with the previous eight or nine years. Not all strains of hæmolytic streptococci are susceptible to the action of sulphanilamide. Hoare,[(1)] in a very careful study of bactericidal changes induced in human blood and serum by "Prontosil" and sulphanilamide, found among twenty-one strains two group *A* strains which were not susceptible to its action *in vitro*. Both these strains came from human puerperal infections that failed to respond clinically to sulphanilamide. They were, moreover, both avirulent in mice.

Method of Treatment by Sulphanilamide of Puerperal or Post-Abortal Hæmolytic Streptococcal Infections.

Oral Administration.

The diagnosis should be established bacteriologically by lochial swabbing or blood culture, or both.

In severe infections, when the organism has invaded beyond the uterus, the object of treatment is to attain and maintain a concentration of 1 in 10,000 to 1 in 7,000 of sulphanilamide in the blood; that is, 10 to 13 milligrammes per 100 cubic centimetres. Oral administration is the method of choice. An adult weighing 45·4 kilograms (100 pounds) or more should receive an initial dose of five grammes of sulphanilamide. The maintenance dose should consist of one gramme commenced four hours later and continued at intervals of four hours; that is, six grammes should be given in each twenty-four hours.

Quantitative estimation of free sulphanilamide in the blood should be made during the first twelve hours and possibly later. If the concentration is below 10 milligrammes per 100 cubic centimetres with these doses, or if the patients have nausea or vomiting, or are comatose, administration by mouth being impracticable, the parenteral routes may be used.

Parenteral Administration.

Pure sulphanilamide, a white crystalline substance, is soluble in normal saline solution. A suitable form obtainable in Sydney is Burroughs Wellcome and Company's "Sulphonamide-P"; 0·8 gramme is dissolved in 100 cubic centimetres of boiling saline solution and allowed to cool. The solution should be made fresh daily. The daily dose for an adult is 400 to 500 cubic centimetres, administered subcutaneously or by the slow intravenous drip method. The disodium salt, "Prontosil Soluble", is also available. It is supplied as a 5% solution in ampoules (Bayer). Although the manufacturers suggest a daily dose of 25 cubic centimetres, many American authors recommend much larger doses in severe infections. A reasonable standard is 0·5 cubic centimetre per pound of body weight, administered intramuscularly. In less severe infections the same initial dose should be given, followed with a maintenance dose of two to four grammes daily. Reduce the dose as clinical improvement occurs, but continue with a small dose for four or five days after the patient is afebrile. Large doses should not be continued for longer than ten days, for if there is no clinical improvement within that time it is unlikely to occur. During the administration of sulphanilamide a routine such as the following is advised:

1. Give no aperients other than liquid paraffin or some paraffin emulsion.
2. Give enemata if necessary.
3. The patient should have a low-residue diet.
4. During the excretion of sulphanilamide the reabsorption of sodium and potassium from the renal tubules is said to be interfered with, so alkalis are required to replace this loss. Bicarbonate of soda, 0·6 gramme (10 grains) should be given with each dose of sulphanilamide.
5. Other synthetic compounds, such as aspirin, phenacetin, "Veramon" or the barbiturates, should be withheld.
6. Prohibit sulphur-containing foods, such as onions and eggs.
7. Withhold sulphates, for example, magnesium sulphate and ferrous sulphate.

In addition, it must be stressed that the administration of sulphanilamide is only a part of the general treatment of the patient.

Dr. Durie in her paper has dealt with toxic manifestations that may occur and the methods of dealing with them; but since we have adopted the routine described above severe toxic symptoms have been rare.

The Use of Sulphanilamide in Infections by Other Organisms.

To return to our table of infecting organisms. Should sulphanilamide be used in infections by other organisms than the streptococcus? Colebrook and Purdie[2] state that in their view there is abundant support for the continued use of sulphanilamide in puerperal infections by hæmolytic streptococci, but not for its use in similar infections due to other organisms. There are no reports of experimental or clinical evidence to suggest its use in infection by anaerobic streptococci, *Streptococcus viridans* or aerobic non-hæmolytic streptococci. With regard to the *Bacillus coli* group, it has been known for some time that these organisms are susceptible to the action of sulphanilamide in the urine. The bactericidal effect on the *Bacillus coli* of the urine of patients treated with sulphanilamide has been investigated by many workers. Kenny[3] *et alii* demonstrated (*a*) variations in susceptibility of different strains, and (*b*) an increase in the bactericidal action with a higher concentration of sulphanilamide. Kenny[3] and co-workers used 17 different strains of coliform bacilli and made cultures in specimens of urine having a sulphanilamide content varying between 3 and 24 milligrammes per 100 cubic centimetres. They obtained either bacteriostasis or sterilization in nearly 40% of 48 experiments. Now, since it is possible to obtain these concentrations clinically in the blood, a bacteriostatic action in the tissues, on some strains at least, might be expected. For this reason I think a trial of sulphanilamide is warranted in septicæmia or peritonitis due to the *Bacillus coli*.

E.M.B., aged thirty-seven years, developed septicæmia following an abortion due to interference. *Bacillus proteus* was grown on culture from her blood. For six days her temperature varied between normal and 40·5° C. (105° F.) and she appeared very ill, although not critically so. One gramme of sulphanilamide was administered four-hourly for forty-eight hours and then six-hourly for the following two days. Pronounced clinical improvement took place during this period of treatment. Six days later much necrotic placental débris was removed from the uterus, with subsequent normal convalescence.

Staphylococcal Infections.

The difficulty in studying the staphylococcus experimentally has been to find a strain of sufficient and constant virulence, so that the untreated control animals died with some regularity. Domagk[4] had favourable results in experimentally induced rabbit infections, and Buttle[5] was successful in protecting mice against a virulent bovine strain by administering almost toxic doses. Variable clinical results in human infections have been reported. Colebrook and Purdie[2] report recovery in two of three gravely ill patients, all with positive blood cultures. These patients received massive doses of sulphanilamide. Three patients with staphylococcal infections, one with septicæmia and two with peritonitis, have been treated with "Uleron" at the Women's Hospital. The one patient who recovered had laparotomy and free drainage of the peritoneal cavity. These patients, however, all received quite inadequate doses. In view of the extreme gravity of generalized *Staphylococcus aureus* infections, in my opinion the administration of very large doses of sulphanilamide is justified. One of Colebrook's[2] patients, treated

at Queen Charlotte's Hospital, was given the tremendous dose of 34 grammes (16 grammes by the intravenous drip method) during the first twenty-four hours, followed by 15 grammes a day. No toxic effect was observed.

Clostridium Welchii Infections.

It is becoming generally recognized that the *Clostridium welchii* is responsible for a fulminating and generally fatal infection following abortions and deliveries associated with much interference. There is some experimental evidence that sulphanilamide exerts a bacteriostatic action on this organism. Injection of *Clostridium welchii* into the peritoneal cavity or the tail vein of the mouse leads to its rapid death. Long and Bliss[6] have been able to demonstrate the inhibition of its growth in the peritoneal cavity of the mouse by the action of sulphanilamide. In further experiments[7] a varying percentage of mice have been enabled to survive an intravenous injection of a lethal inoculum by treatment with sulphanilamide begun one hour later. These experiments are important, and suggest the use of sulphanilamide in human infections. The mortality rate from this organism, once its invasion extends beyond the uterine cavity, is so high and the course of the disease is so rapid that desperate means are justifiable. I have not yet had an opportunity of using it in this infection, but suggest a massive initial dose in conjunction with gas gangrene antiserum. It would be necessary for maintenance doses to be controlled by quantitative blood estimations, since renal efficiency is very much impaired by the toxins of the *Clostridium welchii*. Summing up, we may say that in hæmolytic streptococcal infections the use of sulphanilamide by the method indicated is established. With generalized infections by staphylococci, the coliform bacilli and the *Clostridium welchii*, it seems to me that there is enough evidence to warrant its use where conditions are such that the treatment can be carefully controlled by laboratory methods. Full clinical records of its use in these infections should certainly be published.

The Prophylactic Use of Sulphanilamide.

Should sulphanilamide be used prophylactically? With a few exceptions, to be referred to later, I think not. In the first place, on account of its rapid elimination, administration would need to be continued over a period. Kenny[8] found that two patients who were receiving sulphanilamide for infections of the urinary trace developed acute tonsillitis, caused by group *A* hæmolytic streptococci. These patients were taking 1·5 grammes per day. Johnstone[8] gave either sulphanilamide or "Proseptasine" to 500 women after labour, but it is doubtful from his data whether it had any useful effect. He himself states that the general results seem to indicate no beneficial effect.

As Colebrook[9] points out, the circumstances in which administration of sulphanilamide prophylactically suggests itself may be considered in the following way. (i) It might be used in normal childbirth, because of the certain small risk of infection in every confinement. This Colebrook regards as unjustified, because the risk of hæmolytic streptococcal infection is small, varying from 1 in 2,000 to 1 in 50, whereas the risk of toxicity from sulphanilamide is appreciable. (ii) It might be administered in deliveries involving interference, that is, operative delivery, internal version, manual removal of the placenta, because the risk of sepsis is greater. Here it would be justifiable if there was evidence that the incidence of hæmolytic streptococcal infections in such cases was greater than among normal deliveries. As he himself states, there is no such evidence. (iii) It might be used in childbirth associated with strongly suspected or known risk of infection by hæmolytic streptococci; for example, a woman delivered in a small maternity hospital, where other women have a high temperature, or where there has been a recent known infection. Again, a patient may have erysipelas, acute tonsillitis or a septic wound at the time of delivery; or she may be confined in a home where a child has a discharging ear or even scarlet fever. An oral dose of one gramme three times a day should be given for at least four or five days.

Sulphanilamide in Pyelitis and Cystitis.

Before concluding I should like to refer to the use of sulphanilamide in pyelitis and cystitis of pregnancy and the puerperium. It is now well recognized that during pregnancy, in most women, dilatation of the pelvis of the kidney and the ureter occurs, varying in degree. Two factors help to bring this about: (i) lack of tone of the ureteral musculature, probably hormonal in origin, and (ii) obstruction of the atonic ureter at the pelvic brim by pressure of the growing uterus. The resulting stasis predisposes to infection, and this occurs in a small proportion of cases. The infecting organism is generally a Gram-negative coliform bacillus. In severe infections the kidney itself is involved (pyelonephritis) and renal efficiency is impaired by urinary back-pressure. The series of patients with pyelitis or pyuria and bacilluria to which I am about to refer, have not been selected and have been consecutive patients at the Women's Hospital this year. All the tests on the urine have been made in the pathology department. The numbers of pus cells per high-power field have been counted and the organisms identified after culture. In all the cases referred to below the infecting organism was a coliform bacillus.

TABLE II.

Sixteen Patients with Pyelitis or Pyuria and Bacilluria Not Treated with Sulphanilamide.

Stage at which Infection Occurred.	Febrile Patients, with Clinical Signs of Pyelitis.	Afebrile Patients, with Pronounced Pyuria and Bacilluria.
Ante partum	11	2
Puerperium	1	2

The treatment consisted in the administration of alkalis and "Mandelix". Eserin sulphate was given hypodermically. The ureters were catheterized when necessary.

The urine was rendered sterile in four cases, that is, in 25%. Surgical induction was carried out in two cases, and premature labour occurred in one case. In these three cases the infants died.

TABLE III.

Twenty-Four Patients with Pyelitis or Pyuria and Bacilluria Treated with Sulphanilamide.

Stage at which Infection Occurred.	Febrile Patients, with Clinical Signs of Pyelitis.	Afebrile Patients, with Pronounced Pyuria and Bacilluria.
Ante partum	12	9
Puerperium	3	0

The urine was rendered sterile in every instance. A return of the bacilluria was common, but no return of clinical symptoms occurred. There were no stillbirths or neonatal deaths. Three patients are still undelivered.

The return of bacilluria and even mild pyuria may be due to the fact that the predisposing cause, namely, obstruction to the normal urinary flow, is present throughout the course of pregnancy. The rationale of treatment has been based on the evidence of Helmholz and Osterberg,[10] of the Mayo Clinic, that sulphanilamide has a greater bactericidal effect in an alkaline than in an acid urine. Our object has been to find out how small a dose of sulphanilamide will sterilize the urine.

The following scheme of treatment has been found satisfactory:

1. Give alkalis until the urine is strongly alkaline.
2. Then give 0·5 gramme of sulphanilamide orally four times a day at four-hourly intervals, and continue the alkalis.
3. On the fourth or fifth day a catheter specimen of the urine is usually sterile; and we have found the urinary concentration of free sulphanilamide to be between 40 and 50 milligrammes per 100 cubic centimetres.
4. Then reduce the daily dose of sulphanilamide to one gramme or sometimes to 0·5 gramme, but maintain an alkaline urine.
5. The precautions enumerated above regarding aperients, diet and drugs *et cetera* are equally important here.
6. All methods for relieving the ureteral obstruction and promoting urinary flow, such as rest in bed, postural exercises, the hypodermic administration of eserin sulphate and ureteral catheterization should, of course, be used, when indicated, in conjunction with sulphanilamide.

Nearly all these patients have become cyanosed in some degree, a few sufficiently so to need a reduction of the dose. One of the most seriously ill patients developed jaundice; but at the same time she had ketonuria from persistent vomiting. Improvement followed ureteral catheterization, and it was found possible to resume sulphanilamide therapy with excellent results. The urine became sterile and the blood count steadily improved during its administration. Early in this series a patient, who had been satisfactorily treated for severe pyelitis, returned three weeks later with profound anæmia, which responded very slowly to treatment. This suggested the advisability of making a blood count at intervals of three or four days during treatment. A very definite decrease in both the red and white cells has been observed in the majority of cases.

The Effect of Sulphanilamide on the Erythrocyte Count.

Of fourteen patients with pyelitis of pregnancy treated with alkalis and sulphanilamide, the erythrocyte count of four patients was unaffected or rose slightly, and that of ten patients decreased. The results in these ten cases are shown in Table IV.

TABLE IV.

Results of Sulphanilamide Therapy in Ten Cases of Pyelitis of Pregnancy.

Average Decrease in Erythrocytes.	Extremes of Decrease in Erythrocytes.	Average Number of Days of Treatment.	Extremes of Time of Treatment.
694,000	40,000 to 1,570,000	7	3 to 15 days.

Most of these patients had a moderate leucocytosis as a response to the infective process; and in almost every instance after the administration of sulphanilamide there has been a rapid fall towards the normal count, but not beyond. This behaviour of the leucocytes has been observed by other observers[11] to occur in various febrile conditions treated by sulphanilamide; but I have not found reference anywhere to a fall in erythrocytes after such small doses of sulphanilamide and occurring so consistently. I should like to know if it occurs only in pregnancy or if it is connected in some with the nature of the infecting organism. However, the practical point is that when acute pyelitis of pregnancy is being treated in this manner repeated red cell counts are necessary to control the dosage and length of administration.

Conclusion.

The introduction of sulphanilamide has set us many interesting problems to solve, and this paper has touched on only a few of them. No doubt before half of them are solved the advent of some new chemotherapeutic substance will bring a new set of problems for the perplexed practitioner.

Acknowledgements.

I wish to thank the members of the honorary medical staff of the Women's Hospital, Crown Street, for allowing me to see some of their patients. My thanks are also due to Dr. Durie and her staff in the pathology department for undertaking the many tests on the patients referred to in this paper; in particular I should like to thank Miss McLaren, who made the numerous blood counts.

References.

(1) E. D. Hoare: "Bactericidal Changes Induced in Human Blood and Serum by Sulphamido-Chrysoidine and Sulphanilamide", *The Lancet*, Volume I, 1938, page 655.
(2) L. Colebrook and A. W. Purdie: "Treatment of 106 Cases of Puerperal Fever by Sulphanilamide", *The Lancet*, Volume II, 1937, pages 1237 and 1291.
(3) M. Kenny, E. D. Johnston and T. von Haebler: "p-Aminobenzenesulphonamide in Treatment of Bacterium Coli Infections of the Urinary Tract", *The Lancet*, Volume II, 1937, page 119.
(4) G. Domagk: *Deutsche medizinische Wochenschrift*, Volume LXI, 1935, page 250 (quoted by W. L. Holman and G. L. Duff, "Sulphanilamide and Similar Compounds in Chemotherapy", *The American Journal of the Medical Sciences*, Volume CXCV, March, 1938, page 379).
(5) S. A. H. Buttle, H. J. Parish *et alii*: "The Chemotherapy of Typhoid and some other Non-Streptococcal Infections in Mice", *The Lancet*, Volume I, 1937, page 681.
(6) E. A. Bliss and Perrin Long: "Observations on the Mode of Action of Sulphanilamide", *The Journal of the American Medical Association*, Volume CIX, 1937, page 1524.
(7) P. Long and E. Bliss: "Observations upon the Experimental and Clinical Use of Sulphanilamide in the Treatment of Certain Infections", *The Canadian Medical Association Journal*, Volume XXXVII, Number V, 1937, page 457.
(8) R. W. Johnstone: "Prophylactic Use of Sulphonamide Preparations in Obstetric Practice", *The British Medical Journal*, March 12, 1938, page 562.
(9) L. Colebrook: "Prophylactic Treatment in Obstetrics by Means of 'Prontosil' and Sulphanilamide", *The Lancet*, Volume II, 1937, page 286.
(10) H. F. Helmholz and A. E. Osterberg: "The Effect of pH of the Urine on Concentration of Free and Conjugated Sulphanilamide Necessary for Bactericidal Action", *Proceedings of the Staff Meetings of the Mayo Clinic*, Volume XII, 1937, page 661.
(11) John A. Bigler *et alii*: "The Leucocyte Response to Sulfanilamide", *The Journal of the American Medical Association*, Volume CX, Number 5, 1938, page 343.

"Q" FEVER: FACTORS AFFECTING THE APPEARANCE OF RICKETTSIÆ IN MICE.[1]

By F. M. BURNET AND M. FREEMAN.

(From the Walter and Eliza Hall Institute of Research in Pathology and Medicine, Melbourne.)

MICE infected with the Rickettsia of "Q" fever show no recognizable symptoms, and the fact of infection can be established only by killing the animals at a suitable period after inoculation and examination of the smears from liver and spleen. Our general experience has been that mice killed about seven days after inoculation with a large amount of infective material provide heavily infected organs, but that with small doses the appearance of the Rickettsiæ is delayed. There were two practical reasons why it seemed important to know as accurately as possible the relation between the size of dose administered and the time of maximum abundance of Rickettsiæ in the organs. In the first place, it is necessary to have very heavily infected tissues for the preparation of rickettsial agglutinating emulsions (Burnet and Freeman, 1938), and at times we have found it difficult to obtain these with regularity. An entirely different problem is presented when mice are inoculated with blood from a patient suspected to be suffering from "Q" fever. The numbers of Rickettsiæ in the inoculum will be very small, and if mice are killed too early, a positive diagnosis may be missed.

[1] Work carried out under grants for research on virus diseases from the Rockefeller Foundation and from the National Health and Medical Research Council.

With these problems in view, a series of experiments have been carried out on some of the factors which influence the numbers of Rickettsiæ appearing in inoculated mice. The three factors with which we have been concerned are the dose of infective material inoculated, the influence of antibody present in the inoculum, and the effect of preliminary irradiation of the mice.

The Influence of the Size of the Dose on the Time of Appearance of Rickettsiæ.

The experiments on the influence of dose may be divided into two sets, although they were actually done concurrently. The object of the first was to find the time at which Rickettsiæ appeared in the liver and spleen of mice inoculated with serial tenfold dilutions of infective spleen emulsion. The results with the limiting infective dilutions might be expected to offer an indication as to the best period for examining mice inoculated with blood or other material suspected to be infective. The second set was concerned with the disappearance of Rickettsiæ from mice receiving a heavy inoculum, as judged both from smears and from the results of subinoculation to other mice.

Method of Experiment.

The inoculum for a whole series of experiments was prepared by grinding with sterile quartz powder two mouse spleens in smears from which numerous Rickettsiæ were found. The smooth paste was suspended in saline solution containing 10% of filtered normal horse serum, and the quartz powder was allowed to settle. A series of tenfold dilutions, also in horse serum-saline solution, was made from this emulsion, and amounts of 0·25 cubic centimetre were inoculated intraperitoneally into mice eight weeks old. These were killed at intervals over a period of five weeks. Smears from spleens and livers of all mice were stained by Castaneda's method and examined for Rickettsiæ. In the case of the mice receiving the undiluted inoculum, samples of blood were taken from the axillary artery and the serum was tested for agglutinins. Subinoculations of undiluted spleen emulsions from most of these mice were also made, usually into six mice which were killed at successive intervals after inoculation.

The time taken for Rickettsiæ to appear after progressively smaller doses is shown in Table I. It

TABLE I.

Dilution of Inoculum and Appearance of Rickettsiæ in Mice.

Dilution of Emulsion.	Number of Days After Inoculation.	Presence of Rickettsiæ in Smears.	
		Spleen.	Liver.
0	7	++,[1] +[2]	+, ++
10^{-1}	7	++, +, +	+, +, +
10^{-2}	7	++, +, +	++, +, +
10^{-3}	7	−, −	−, −
	11	+, −	−, −
	14	−, −	+, −
10^{-4}	11	+, −	++, −
	14	−, −	−, −
	21	−, −	−, −
10^{-5}	11	−, −	−, −
	14	+, −	+, −
	21	−, −	−, −
10^{-6}	14	−, −	−, −
	21	−, −	+, −
	28	+, −	+, −

[1] ++ = Rickettsiæ found in every two or three microscopic fields.
[2] + = Rickettsiæ present in small numbers.

will be seen that with dilutions beyond 1 in 100 there is an increasing delay, and the Rickettsiæ are present in smaller numbers. In both this and a duplicate experiment the highest dilution tested (10^{-6}) gave rise to Rickettsiæ in three to four weeks.

The changes which follow inoculation with a large amount of infective material are shown in Table II. The results, which have been confirmed by a similar experiment, may be summarized as showing that the number of Rickettsiæ visible in smears from the spleen is at a maximum on about the seventh day after inoculation. Thereafter the numbers diminish considerably, but some can be found up to the twenty-first day. Despite the presence of visible Rickettsiæ, spleens removed at fourteen and twenty-one days are not infective to fresh mice, as far as can be judged from examination of smears at successive intervals. Evidence that a low-grade infection may nevertheless occur has been obtained on several occasions by the late appearance of antibodies in the serum of mice. In one experiment, no Rickettsiæ and no antibodies were found in mice inoculated with an emulsion of a spleen taken on the nineteenth day and killed at nine and sixteen days respectively; but in one killed in twenty-three days there was an agglutinin titre of 1 in 100, although there were still no Rickettsiæ. This was also the case with mice killed thirty and thirty-seven days after inoculation. The results of agglutinin titrations provide a possible explanation for these discrepancies. Antibodies are present from the seventh day, and reach a high titre (1 in 100) by the fourteenth day. A spleen emulsion from a mouse killed on the fourteenth or twenty-first day will obviously contain, in addition to Rickettsiæ, considerable amounts of antibody which may be capable of preventing or masking infection. Experiments to determine whether relatively small amounts of immune serum could prevent infection by small numbers of Rickettsiæ were therefore carried out. Positive results were obtained, which are described in the next section.

The Protective Action of Immune Serum.

Pooled samples of sera from six controls and six mice with "Q" fever were used. The latter had been inoculated three weeks previously, and the agglutination titre of the pooled serum was 1 in 100.

A spleen emulsion from a mouse with "Q" fever was diluted to 1 in 100 with broth. This dilution was chosen as the highest dilution of Rickettsiæ giving positive results on subinoculation to mice in seven to ten days. Equal volumes of tenfold dilutions of the sera to be tested were mixed with this emulsion and allowed to remain for one hour in the refrigerator before inoculation into mice. Four mice were inoculated intraperitoneally with each mixture. They were killed after ten days, and smears of their spleens and livers, stained by Castaneda's method, were examined for the presence of Rickettsiæ.

TABLE III.
Protection Tests with Mice.

Source of Serum.	Dilution of Serum.	Presence of Rickettsiæ in Mice.
Control mice	10^{-1}	++,[1] +,[2] +. 1 dead.[3]
"Q" fever mice	10^{-1}	−, −, −, −
	10^{-2}	−, −, −. 1 dead.[3]
	10^{-3}	+, +, +, +

[1] ++ = Rickettsiæ found in every two or three microscopic fields.
[2] + = Rickettsiæ present in small numbers.
[3] Non-specific deaths, probably due to infection by a *Bacillus pseudotuberculosis rodentium*.

It is readily seen that the serum from mice previously inoculated with "Q" fever is capable of protecting further mice from infection.

Similar experiments have been carried out with immune human and bandicoot sera in connexion with other work which will be reported in association with Dr. Derrick. Sera from both species may have a power to prevent infection of the same order as that found with immune mouse serum.

The Treatment of Mice with X Rays before Inoculation.

Zinsser and Castaneda (1932) found that preliminary irradiation with X rays greatly increased the numbers of typhus Rickettsiæ which appeared

TABLE II.
Presence of Rickettsiæ, Agglutinating Titre and Infectivity in Mice.

Number of Days After Inoculation.	Presence of Rickettsiæ in Spleen.	Agglutinating Titre.				Infectivity of Spleen to Fresh Mice.	
		1 : 10.	1 : 30.	1 : 100.	1 : 300.	Number of Days After Inoculation.	Presence of Rickettsiæ in Spleen.
7	++	++	±			7	+, +, −
11	+	+++	++	−		7	−, −
						14	+, −
						19	−, −
14	±	+++	+++	+	−	12	−, −
						18	−
						25	−
						32	−
						40[1]	−
21	±	+++	+++	+++	+	11	−
						18	−
						25[1]	−
						32	−
						38[1]	−, −
28	−	+++	+++	+++	++	..	..
35	−	+++	+++	+++	++	..	..

[1] The sera of these mice were tested for agglutinins and found to be positive.

in the peritoneal exudate of inoculated rats. In the hope of increasing the yield of "Q" fever Rickettsiæ, several experiments with irradiated mice have been carried out. In general, somewhat larger numbers of Rickettsiæ were found in spleen smears from the treated mice, but this improvement was counterbalanced by the fact that the spleens were usually much reduced in size. The total amount of rickettsial emulsion obtainable was not significantly increased.

When mice about eight weeks old were used, a dose of 1,200 *r* resulted in the death of about half the mice; but all survived 900 *r*. Mice receiving these doses had small spleens, but more Rickettsiæ appeared in the smears than in smears from control mice receiving the same inoculum. When mice which had received 600 *r* were inoculated, the spleens were normally enlarged, and there were somewhat larger numbers of Rickettsiæ than in control mice. In none of the treated animals were the numbers greater than can often be obtained from normal mice.

The most definite result was obtained in an experiment with fully grown mice, seventeen weeks old. Such mice normally yield few Rickettsiæ. Eight were irradiated with 900 *r*. There were five deaths; but in smears from the spleen and liver of the three survivors numerous Rickettsiæ were found. The control mice of the same age were very lightly infected, no Rickettsiæ appearing in smears from three of the eight.

Discussion.

From these experimental results it appears that the best method of using mice for the isolation of "Q" fever Rickettsiæ from human blood or other suspected material is to inoculate six or eight mice intraperitoneally. Two should be killed on the tenth and fourteenth days after inoculation, and spleen and liver smears should be examined. The remainder should be kept for three to four weeks and then bled for serum. Positive agglutination with rickettsial emulsion will provide final evidence that the mice were specifically infected.

For the production of agglutinating emulsion for which very heavy infections are needed, the requisites are to use young mice six to eight weeks old, and inoculate them with material from mice which have been inoculated not more than seven days previously. Irradiation has not been of practical value in our hands; but with other stocks of mice or other rickettsial strains it might prove valuable.

Summary.

1. The time at which Rickettsiæ appear in spleen smears from mice inoculated with "Q" fever material depends on the dose administered, being earlier with larger doses.

2. After the optimal period, Rickettsiæ in the spleen and liver rapidly diminish in number and fail to induce demonstrable infection on subinoculation.

3. Agglutinins appear in mouse blood about seven days after inoculation, and serum with high agglutination titre also has a considerable power to protect against infection.

4. Irradiation of mice with just sublethal doses slightly increases the intensity of infection with "Q" fever Rickettsiæ.

Acknowledgements.

We are indebted to Dr. Kaye Scott and to Miss D. Wellington, of the X ray department of the Royal Melbourne Hospital, for the irradiation of the mice used in these experiments.

Bibliography.

F. M. Burnet and M. Freeman: "The Rickettsia of "Q" Fever: Further Experimental Studies", THE MEDICAL JOURNAL OF AUSTRALIA, Volume I, February 12, 1938, page 296.

H. Zinsser and M. R. Castaneda: "A Method of Obtaining Large Amounts of Rickettsia Provaceki by X-Ray Radiation of Rats", *Proceedings of the Society for Experimental Biology and Medicine*, April, 1932, page 840.

OBSERVATIONS ON VULVO-VAGINITIS IN CHILDREN.

By NORMAN M. GIBSON, O.B.E., M.B.,

Honorary Medical Officer for Venereal Diseases, Royal Prince Alfred Hospital, Sydney,

AND

C. J. WILEY, M.B.,

Honorary Surgeon for Venereal Diseases, Royal North Shore Hospital of Sydney.

VULVO-VAGINITIS is an acute inflammatory condition involving the vulva and vagina. It affects children at any period between birth and puberty, and is a source of great anxiety on account of its resistance to treatment and the fear it excites in the minds of the parents. Probably the majority of patients are treated in public institutions. While the gonococcus is responsible for most cases, a number of other organisms also are capable of causing it.

The disorder is very infectious, and is usually caused accidentally by infected sponges or linen or more frequently by infected bath water, especially when this has been contaminated at or about body temperature. This circumstance makes it important to advise adults suffering from the disease on suitable precautions to take to avoid creating possible sources of infection.

Various circumstances contribute to the vulnerability of children to this infection. For one thing, the vulva of a child is more exposed than that of an adult because the *labia majora* have not developed; for another, there are differences in the histological structure of the affected parts in children compared with those of adults. The mucous membrane in children is thin and is not protected as in the adult by thick layers of stratified squamous epithelium. In early life the vaginal secretion is alkaline, but with approaching puberty there is an alteration in its amount and character. The secretion becomes acid, and Döderlein's bacillus appears. This combination of circumstances makes accidental infection much less probable.

The incubation period is probably similar to that in the adult, namely, from two to ten days, and most frequently three or four.

Clinical Signs and Symptoms.

Gonococcal vulvo-vaginitis is extremely painful, and the amount of pus is considerable. The most striking feature in early cases is the œdema of the tissues. Frequently the secretions stain the child's clothing, and this circumstance is not infrequently the cause of the mother's attention's being drawn to the child. Occasionally pain on micturition is a complaint. The inflammatory condition involves vagina, hymen, vestibule, clitoris, labia and sometimes urethra. An intertrigo of the genito-crural folds is the rule.

The gonococcus may be demonstrated in smear and culture. In the collection of specimens, superficial discharges are removed and a platinum loop is passed well into the vagina. Smears are best stained by Gram's solution and cultures made on 2% glucose-serum agar. The clinical signs, however, are usually distinctive. In non-gonococcal cases the most distinctive feature, when the patient is seen in the early stages, is the absence of œdema, the secretions being less purulent and more mucoid in character and the intensity of the inflammatory process being much less pronounced.

In infections caused by the gonococcus the intensity of the signs and symptoms gradually lessens. The acute stage is often a long one; but in due course the gonococcus tends to disappear and to be replaced by secondary invaders. If the patient is first seen at this stage, accurate diagnosis may be difficult. The natural tendency is to spontaneous cure; and this ultimately ensues, probably whether the patient is treated or not.

Course.

The course of the disease is usually protracted; sometimes it persists for years. This circumstance is a source of great anxiety to the parents, who see in the persistence of the inflammation a threat to the future welfare of the child. It is advisable to warn the parents that treatment is likely to be protracted and to give them an assurance that permanent damage is unlikely and that the ultimate result will be a happy one.

Complications.

The disease has usually been thought to be uncomplicated. According to McDonagh,[1] Bartholinitis does not occur. The cervix is possibly infected more often than has been suspected in the past, as examination of this area is not always made. We have found that examination, if required, may conveniently be made with the short male urethroscope. Ascending infection through the internal os, causing endometritis and salpingitis, is reputed to be rare, but nevertheless it does occur. Over the course of some years we have seen three patients with salpingitis complicating this disease.

Treatment.

Special attention must be paid to the avoidance of possible infection of other children. In a family with other female children, the affected child should either have a separate bath or else be bathed last. Afterwards the bath should be carefully washed with cold water or a disinfectant and allowed to dry before being again used.

Rest in bed, preferably in the open air, is the most satisfactory measure during the first four weeks of a gonococcal infection. It has the advantage of relieving the soreness of the vulva and of rendering possible extension of the disease less likely. A suitable diet should include milk, fruit and fresh vegetables. It is an advantage to order a hot hip bath for fifteen minutes twice a day. Douching, especially with permangate of potash solutions, in our experience is not advisable. Instillations into the vagina of a 0·25% solution of "Protargol" are preferable.

Thomson[2] suggests the application of remedies in certain cases through a urethroscopic tube. We have found that the most satisfactory local treatment is to fill the vagina once a day with an ointment prepared with a base of olive oil, vaseline and lanoline, and containing 2% "Mercurochrome". It should have a semi-fluid consistency. A special collapsible tube containing the ointment and fitted with a three-inch nozzle should be used for applying this treatment. The nozzle is inserted into the vagina, which is filled with the preparation. A light pad of non-irritating material is worn by the patient in order that the clothing may not be soiled by the ointment. Any movement of the patient squeezes some of the preparation into the vulval cleft. This area is thus continuously in contact with the remedy. A further advantage of this line of treatment is that it can be easily applied by the mother.

Vaccine Therapy.

Vaccines should not be used in the two or three weeks following the onset of the disease, as satisfactory results follow only after the patient has developed some natural immunity.

In gonococcal infections a detoxicated vaccine should preferably be employed. The method of preparation is to dissolve a suspension of organisms, reprecipitate, and suspend the stroma. The advantage is that this vaccine can be given in large doses. Sensitized vaccines are also efficacious. As sensitization effects an antibody combination with the organism *in vitro*, it is possible to administer this remedy also in considerable quantity without provoking undue reaction in the patient.

Synthetic Remedies.

The use of synthetic remedies is still on its trial. Sulphanilamide, and a later preparation issued by Bayer Pharma Proprietary, Limited, called "Uleron", are useful in some cases of gonococcal infection in adults, but we are without experience

of its use in children. The latter preparation is less toxic. Like vaccines, this mode of treatment gives satisfactory results only when the patient has developed some considerable natural immunity.

Œstrin.

Some favourable reports have been made on the use of œstrin.[3] Oral administration is reputed to be satisfactory in children. The important feature of its use is the appearance of squamous epithelial cells and Döderlein's bacillus in the secretions. Apparently its employment can also be attended by some other effects, such as engorgement of the breasts and vaginal hæmorrhage. Nevertheless, in the opinion of some observers, the drug has great value.

The Standard of Cure.

Reference has already been made to the intractable character of vulvo-vaginitis in children. Relapses are not uncommon, and in gonococcal vulvo-vaginitis the organism may disappear for long periods of time. If this fact is fully realized, the result of smears and cultures will be seen in its right perspective. The position of the complement fixation test is not fully determined; but it may be assumed, on analogy with the adult, that the disappearance of a positive reaction is suggestive of cure. After all, the path of clinical experience is the safest to tread, and continued observation after apparent clinical cure is certainly advisable. It is a comforting reflection, and parents appreciate an assurance on this point, that the disease does not outlast puberty.

References.

(1) J. E. R. McDonagh: "Venereal Diseases", page 339.
(2) D. Thomson: "Gonorrhœa", page 474.
(3) "Report of the Departmental Committee Appointed by the Medical Officer of Health to the County of London", *The British Medical Journal*, Volume I, April 30, 1938, page 961.

SPERMATORRHŒA IN TRICHOSURUS VULPECULA AND OTHER MARSUPIALS.

By ADOLPH BOLLIGER and A. L. CARRODUS.

(*From the Gordon Craig Urological Research Laboratory, Department of Surgery, University of Sydney.*)

IN connexion with our work on the action of sex hormones on marsupials it was noticed that an occasional sample of urine obtained from a male possum (*Trichosurus vulpecula*) contained spermatozoa. We further investigated this finding by observing four male possums over a period of three months. Also the urine of two other marsupials, the bandicoot and the rat-kangaroo, was examined.

Method of Collecting Urine.

As a manifestation of fear, possums and other marsupials frequently void urine on handling. By this method urine is sometimes obtained from animals new to the laboratory surroundings. However, some possums can almost be trained to pass urine as required; for example: one male, number 52, whenever picked up and placed on a vertical mesh wire fence, passed urine. In other cases it is sometimes necessary to massage or press on the lower part of the abdomen in order to start micturition. By these methods as much as 50 cubic centimetres of clean urine can be collected in one handling, and most observations were made on specimens obtained in this manner. Finally, some of the possums and the other marsupials examined were placed in metabolism cages and the urine was collected in this manner. A drop of the fresh uncentrifuged urine was then examined microscopically.

Results.

POSSUM 52.—The animal was a male, weighing 2·5 kilograms. Examination of the uncentrifuged urine on July 11, 1938, showed numerous spermatozoa. Then daily urine examinations for one month revealed with one single exception spermatozoa which varied from less than one to twenty and more per low-power microscopic field. At the end of this period a count was made of spermatozoa in a fresh sample of uncentrifuged urine. On this occasion 200 spermatozoa were found in one cubic millimetre. After this the animal was used for another purpose.

POSSUM 57.—A full-grown male was examined a few hours after its capture in the bush on July 18, 1938. Its urine contained numerous spermatozoa. This finding persisted for three weeks. After this the animal was used for another purpose.

POSSUM 58.—Examination of the animal's urine failed to show spermatozoa on its arrival at the laboratory on July 20, 1938; but spermatozoa were found at subsequent examinations. Since then their presence had persisted for eleven weeks, as shown by half-weekly examinations. The last examination was made on October 10, 1938.

POSSUM 59.—The body weight of the animal was 2·2 kilograms on September 25, 1938. Immediately after its arrival in the laboratory the urine of this animal was found to contain spermatozoa, and at every one of six subsequent urine examinations, spaced over a period of three weeks, spermatozoa were found. The last examination was made on October 12, 1938. On several occasions the urine of one act of micturition was collected in five consecutive tubes. The portion obtained at the end of the micturition contained fewer spermatozoa than the earlier portions.

BANDICOOT (*Perameles nasuta*) 105.—On July 27, 1938, twenty-four hours after its capture in a suburban garden, the animal was placed in a metabolism cage. Two subsequent specimens of urine were collected and both contained spermatozoa. The spermatozoa of *Perameles nasuta* are more than twice as long as those of *Trichosurus vulpecula*.

RAT-KANGAROO (*Caloprymnus campestris*).—The animal was kept at the Zoological Gardens of Sydney. On September 9, 1938, it was placed in a metabolism cage and a specimen of about 150 cubic centimetres of urine was collected. It contained spermatozoa, which were about equal in size to those of *Trichosurus vulpecula*.

The Structure of Spermatozoa as Found in the Urine of Trichosurus Vulpecula.

Von Korff[1] has studied the spermatogenesis in *Phalangista vulpina*. The spermatozoa which he observed in the epididymis he considered as fully developed, and he depicted them as having a spade-shaped head with a prolongation of the cytoplasm along the axial filament from the head to the

centriolar ring. Beyond this he described a long flagellated tail. In general, the spermatozoa as found by us in the urine correspond with the description of von Korff. However, the head, viewed on the flat, appeared broader than that depicted by von Korff, and sometimes had the shape of an arrowhead. In many of the spermatozoa also there is a protoplasmic drop, whose site varies, in the tail. The majority of spermatozoa have lost their motility. A few, however, are still moving about in a sluggish fashion.

Discussion.

The spermatorrhœa as observed in possums and in other marsupials may be considered as an abnormality due to change in environment, diet and possibly handling. This, however, seems unlikely, because spermatorrhœa was detected in new arrivals from the bush as well as in specimens which had been in the laboratory for several months and which seemed to urinate without any manifestation of fear. All this would indicate that under natural conditions also spermatorrhœa is a frequent happening in the marsupials examined and probably in marsupials in general. The possums whose urine was found to contain spermatozoa on so many occasions did not appear to suffer any ill health from this apparently very wasteful loss. They were observed in the winter months, July and August, and in the spring, namely, September and October. The question arises: does spermatorrhœa occur throughout the year? Further observations will settle this question definitely.

As to the cause of the persistent spermatorrhœa observed in possums we offer a tentative explanation, which rests on an anatomical basis.

Oudemans,[2] confirming the findings of previous workers, pointed out that marsupials possessed no seminal vesicles and no ampulla in the *vas deferens*. This statement is still accepted. Therefore, if we assume that the normal adult male produces spermatozoa almost constantly in its comparatively large testicles, then they may be in the first place stored in the epididymis, as already suggested by Cowper[3] with regard to *Didelphys virginiana* (1704). Further on, the narrow *vas deferens* offers little facilities for storage. However, in marsupials there is a widening of the urinary channel, which begins abruptly just above the point where the *vasa deferentia* enter. It may now be assumed that the spermatozoa escape into the dilated portion of the urethra and are flushed out in the act of micturition. Whether this migration of spermatozoa into the urethra is a more or less constant one or occurs during the act of micturition cannot be decided yet with certainty.

Summary.

Spermatorrhœa has been observed to occur in *Trichorsurus vulpecula* for a period of three months. It has also been observed in other marsupials in isolated urine examinations.

A tentative anatomical explanation of the spermatorrhœa as observed in marsupials has been given.

References.

(1) K. von Korff: *"Zur Histogenese der Spermien von Phalangista vulpina", Archiv für Mikroskopische Anatomie*, Volume LX, 1902, page 232.
(2) J. The. Oudemans: *"Die Accessorischen Geschlechtsdrüsen der Säugethiere", Natuurkundige Verhandelingen van de Hollandsche Maatschappij der Wetenschappen*, 1892, page 15.
(3) W. Cowper (1704), as quoted by A. H. Young: "The Male Generative Organs of the Koala", *The Journal of Anatomy and Physiology*, Volume XIII, 1879, page 309.

BLACKWATER FEVER FOLLOWING THE ADMINISTRATION OF "ATEBRIN".

By CARL E. M. GUNTHER, M.B., B.S., D.T.M. (Sydney),
Field Medical Officer, Bulolo Gold Dredging Limited, Bulolo, Territory of New Guinea.

Previous Cases.

IN 1933, Nägelsbach[1] reported the occurrence of blackwater fever in a woman in labour, following the administration of "Atebrin". In the same year Naumann[2] reported two cases supervening on malaria treated with "Atebrin" and "Plasmochin",[1] and in 1934[3] he quoted eighteen patients with blackwater fever who

> . . . either came to him with the disease or developed it within three days of their coming to him with malaria. The only treatment given was "Atebrin".

Amy, in 1934,[4] quotes a series of cases among Indian troops and followers. There were ten cases with six deaths. Before the hæmoglobinuria set in six patients were receiving quinine, three were receiving "Atebrin", one was receiving quinine followed by "Atebrin", and all received "Plasmoquine".[1]

In 1934, Moir[5] reported two cases following the administration of "Atebrin" and "Plasmoquin Simplex",[1] and Murray[6] a case occurring when quinine and "Plasmochin"[1] compound were given immediately after a full course of "Atebrin".

In 1937, Foy and Kondi[7] reported three cases, one occurring in 1932 and two in 1935. None of the patients had taken quinine up to within two to nine months before the onset, but in all cases it occurred

> . . . either during or after treatment of malaria with normal standard doses of "Atebrin".

A New Guinea Case.

The following notes are from a recent case of my own:

> The patient was a female quadroon, married, aged twenty-three years. She was born in New Guinea and brought up under normal European conditions. She has had malaria all her life, and has always responded well to treatment with quinine. Some years ago she had three attacks which responded to treatment with "Quinoplasmoquine"; she had never had "Atebrin". She has never been absolutely regular in taking quinine prophylactically, and for the last year she has more or less neglected it.
>
> Since 1935 she has been under my supervision. Her last attack of malarial fever was in November, 1935. She was treated successfully with quinine. On my cards her spleen is noted as "not palpable" in April, 1936.

[1] The discrepancies in the spelling of "Plasmoquine" are due to differences in the originals.

She had a miscarriage at about six weeks in January, 1935, and a full-term healthy child in November, 1936. During the seventh month she had moderately heavy albuminuria with concurrent attacks of asthma, which disappeared under treatment. Her confinement and puerperium were normal. She has had no sickness since.

On July 27, 1938, I examined her. She was in the fourth month of pregnancy. All systems were normal and her urine was clear. She was feeling very fit and well. I found her spleen projecting four fingers' breadth below the costal margin; it was hard, but not tender. She had had only three prophylactic doses of quinine during the previous ten days, the last on July 21.

I ordered her a course of "Atebrin", 0·1 gramme (1·5 grains), to be taken three times a day for five days, in the hope that it would reduce the size of her spleen. She had one dose on July 28 and three doses on July 29. She forgot to take her morning dose on July 30.

On the morning of July 30 she felt as well as ever. Suddenly, at 11 a.m., she had a severe rigor, with cramps in the fingers and toes. At noon she passed 90 cubic centimetres (three ounces) of black urine.

When she was examined at 12.30 p.m. she had slight splenic pain and tenderness. Her temperature was 38·4° C. (101° F.). She was not jaundiced. At 12.45 p.m. she passed 140 cubic centimetres (five ounces) of still darker urine.

At 2 p.m. I could find no parasites in her blood.

She was given frequent small drinks of plain water and a solution of 3·9 grammes (one drachm) of sodium bicarbonate to 568 cubic centimetres (one pint) of water. No further "Atebrin" was given. Between noon and midnight of the first day she passed eleven samples, totalling 1·9 litres (67 ounces) of heavily coloured urine. During this period she had two more rigors, after each of which the urine darkened for two or three samples and then became lighter again.

Shortly after midnight she commenced bilious vomiting, and once vomited about 175 cubic centimetres (six ounces) of bright blood. By the morning of July 31 she was moderately jaundiced. During the twenty-four hours she passed thirteen samples of urine, totalling 3·0 litres (104 ounces); she had two rigors; and the bilious vomiting continued. At 5 p.m. her hæmoglobin value was 40% by the Hellige scale, 60% by the Tallqvist scale, and the Van den Bergh test elicited an indirect positive reaction. No parasites were seen.

On August 1 she passed 2·4 litres (84 ounces) of urine in sixteen samples, the last four of which were only slightly pink. There were no rigors, and the vomiting ceased in the evening. She was very hungry, so small amounts of jelly, "Bovril", custard and weak tea were given during the afternoon and night.

By 5 a.m. on August 2 she had passed four samples of urine totalling 598 cubic centimetres (21 ounces), all containing a little blood; but all subsequent samples were clear by the guaiacum test. The jaundice had gone by daylight. The administration of liver extract by mouth was commenced.

During the first three days her temperature fluctuated irregularly between 37·8° C. (100° F.) and 40° C. (104° F.). From the fourth to the seventh day it ranged from 37·5° C. to 38·4° C. (99·5° F. to 101° F.); then it fell to 36·9° C. (98·4° F.), with a midday rise to 37·5° C. (99·5° F.) for the next seven days. It became completely normal only after quinine treatment was well established.

On the eighth day she was given 0·03 gramme (0·5 grain) of quinine bihydrochloride; then on successive days she received 0·1 gramme, 0·2 gramme, 0·4 gramme and 0·5 gramme (1·5, 3, 6 and 7·5 grains). On the thirteenth day, and for the next week, she was given 1·0 gramme (15 grains) per day; then she went back to a regular evening dose of 0·3 gramme (5 grains).

On August 16, the eighteenth day of her illness, her colour and pulse were good. No cardiac abnormality was present and her appetite was ravenous. The hæmoglobin value was 60% by both scales. The uterus was firm, the os was closed, and there was no tenderness. She was allowed up, and on the twentieth day was sent home to rest. She has been very well since. The question of terminating the pregnancy has been under discussion, but it will probably be allowed to go on.[1]

Discussion.

No more than a mention need be made here of the innumerable records of cases of blackwater fever precipitated by quinine, or of the steadily mounting numbers undoubtedly precipitated by "Plasmoquine". The point is that of the cases quoted above, Nägelsbach's, certain of Naumann's, three of Foy and Kondi's, and my own, occurred after "Atebrin" alone had been given, while most of the remainder occurred after "Atebrin" combined with quinine or "Plasmoquine" or both had been given.

The obvious conclusions, already reached by many writers, are that "Atebrin" is not invariably capable of preventing blackwater fever, and that it is occasionally capable of precipitating an attack in the same way as quinine and "Plasmoquine" are known to do. By this I do not mean to imply that I believe that these drugs directly produce hæmolysis; on the contrary, in cases apparently precipitated by quinine I have given "Atebrin" from the onset, "Plasmoquine Compound" on the tenth day after the urine has become clear, and quinine as early as the fourth day after the urine has become clear, without any ill effects. In this recent case I have not the hardihood to try "Atebrin" again, in spite of the great value of such a proceeding from the point of view of knowledge to be obtained.

Steudel[8] gives records of eighteen patients treated with quinine, of whom only three died, although he believes that this is not the best treatment. Foy and Kondi state that although quinine is the probable precipitating cause in the majority of cases of blackwater fever in Greece,

> . . . yet the great majority of these are "treated" during their attack with large doses of quinine, with apparently no ill-effects.

In addition, my observations of the onset in various cases have convinced me that, for example, a drug which can be excreted so rapidly as quinine bihydrochloride, cannot feasibly be regarded as the direct cause of a succession of rigors with progressive hæmolysis over a period of forty-eight hours or more after it has been discontinued. Nor is it reasonable that, in my case quoted above, the "Atebrin" which was taken up till 7 p.m. one day could directly cause the series of five rigors observed from 11 a.m. the next day until 2 p.m. the day after that, even though in many patients "Atebrin" is cumulative in its effect. In my worst cases of "Atebrin" idiosyncrasy there have been no rigors and no hæmoglobinuria, and the symptoms have developed within an hour or so of the taking of the last dose of "Atebrin". All symptoms have passed off well within ten hours.

[1] Since this report was written the patient has been sent to Australia, where, during October, it was found that the uterus was still at the size of about four and a half months. No signs of life being discernible in the fœtus, surgical induction was performed. A dead fœtus was delivered, and the patient made a good recovery.

In this case and in one other of mine it has appeared as if the precipitating element has stirred up a latent malarial infection to a fulminating and irregular attack accompanied by hæmoglobinuria; in all my others it has appeared to have the same effect on what promised to be routine attacks of fever. Foy and Kondi also had one case in which "Atebrin" initiated blackwater fever in a patient with latent malaria only.

References.

(1) E. Nägelsbach: *"Schwarzwasserfieber und Atebrin", Archiv für Schiffs- und Tropen-Hygiene"*, Volume XXXVII, Number 7, 1933, pages 337 to 339.
(2) H. E. Naumann: *"Betrachtungen zum Schwarzwasserfieber", Archiv für Schiffs- und Tropen-Hygiene*, Volume XXXVII, Number 6, 1933, pages 299 to 307.
(3) H. E. Naumann: *"Betrachtungen zum Schwarzwasserfieber"* (conclusion), *Archiv für Schiffs- und Tropen-Hygiene*, Volume XXXVIII, Number 4, 1934, pages 171 to 174.
(4) A. C. Amy: "Hæmoglobinuria: A New Problem on the Indian Frontier", *The Journal of the Royal Army Medical Corps*, Volume LXII, Number 3, 1934, pages 178 to 191.
(5) K. T. Moir: "Blackwater Fever following Atebrin", *The West African Medical Journal*, Volume VII, Number 3, 1934, pages 121 to 123.
(6) A. J. Murray: "Blackwater Fever following Atebrin: Fatal Case", *The West African Medical Journal*, Volume VIII, Number 2, 1934, page 17.
(7) H. Foy and A. Kondi: "Three Cases of Blackwater Fever following the Oral Administration of Atebrin", *Transactions of the Royal Society for Tropical Medicine and Hygiene*, Volume XXXI, Number 1, 1937, pages 99 to 102.
(8) E. Steudel: *"Schwarzwasserfieber und Chinin", Archiv für Schiffs- und Tropen-Hygiene*, Volume XXXIX, Number 7, 1935, pages 277 to 287.

A METHOD OF GIVING BLOOD TRANSFUSIONS TO INFANTS.[1]

By V. L. COLLINS, M.D.,
Medical Superintendent, Children's Hospital, Melbourne.

As one still frequently hears the statement that it is impossible to give a blood transfusion to a small baby, or that no one could introduce a cannula into any vein of some even average-sized infants, it has been considered worth while to describe the method in use at the Children's Hospital. The transfusion of blood in infants is often a life-saving procedure, and a certain method of introducing blood is sure to be welcomed. It is particularly important in the hæmorrhages of the new-born, anæmia and *icterus gravis neonatorum*, and in certain chronic infections associated with anæmia. Inability to perform transfusion promptly in some of these cases is often the cause of death.

During the last three years at the Children's Hospital, Melbourne, there have been among the infants treated by blood transfusion a number weighing 1·8 kilograms (four pounds). At the Women's Hospital, Melbourne, where this method of transfusion has been adopted, a premature baby weighing 0·68 kilogram (one and a half pounds) has been given a transfusion on a number of occasions. So easily and rapidly can the operation be carried out by the method about to be described that I have come to regard it as almost infallible.

[1] Read at a meeting of the Melbourne Pædiatric Society on August 18, 1938.

To be able to perform transfusion on an infant promptly and with certainty, three conditions appear to be necessary: first, the existence of a vein that is constant in position; secondly, a certain means of cannulizing a small vein; and, thirdly, some method of introducing the blood at a pressure greater than gravity. In the method described here, the use of the malleolar vein, a needle and stilet as cannula, and a "Record" syringe with a three-way stopcock supply these requirements.

Apparatus.

The most important piece of apparatus is the needle with stilet (Figure I), which renders the cannulizing of even a small vein a simple procedure. The needle is an ordinary large hypodermic needle (gauge 18, 24 millimetres in length by 1·2 in thickness) shortened to 20 millimetres. The stilet projects four millimetres beyond the end of the needle, which is cut straight across and bevelled around its circumference so that it tapers to the stilet (Figure I, *B*). Thus prepared, the round tip of the stilet, projecting

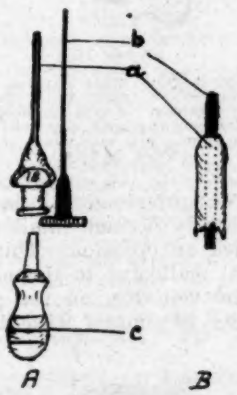


FIGURE 1.
A.: Needle and stilet apart. *B.*: Needle in stilet (enlarged), showing bevelling at tip. *a.*: needle, *b.*: stilet, *c.*: adaptor.

through the needle, can be introduced into a vein and the larger body of the needle will readily follow on into the lumen of the vein. The stilet can then be withdrawn, the needle being left in the vein.

The remainder of the apparatus (Figure III) consists of a three-way stopcock (*e*), a "Record" syringe of 20 or 30 cubic centimetres' capacity, a metal adaptor (*c*), rubber tubing with a lumen of four millimetres' diameter and apparatus for blood-taking. One piece of rubber tubing (*d*), 25 centimetres long, runs from the stopcock to the adaptor, which fits the needle. A second piece of tubing, 30 centimetres long (*g*), connects the stopcock to the vessel containing the citrated blood.

Site of Transfusion.

Because of its constancy in position and the ease with which it can be isolated, the malleolar vein (commencement of the great saphenous vein) is the vein of choice. It passes over the anterior surface

of the medial malleolus, and from here pursues a course posteriorly to the dorsal border of the tibia, along which it ascends. A line taken from the anterior surface of the medial malleolus to a point on the posterior border of the tibia at the upper end of the lower quarter indicates accurately the line of the vein. Under the morning shower bath

FIGURE II.

Subcutaneous inner surface of lower end of right tibia, showing position of the malleolar vein upon the bone. *a.*: medial malleolus, *b.*: malleolar vein. (After Fraser.)

the vein stands out prominently in most individuals, and one can readily become familiarized with its anatomy on such an occasion. During its course from the medial malleolus to the posterior border of the tibia, the vein lies on the periosteum (in Figure II its line of contact with the bone can be

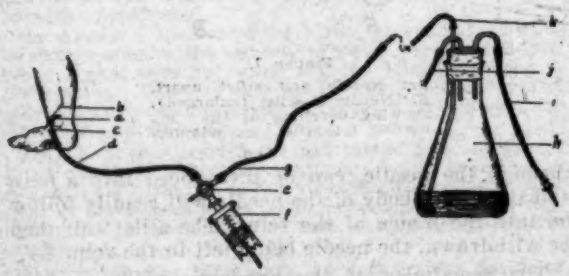


FIGURE III.

Complete apparatus for giving blood transfusion to infants. *a.*: needle in malleolar vein, *b.*: showing course of vein, *c.*: adaptor, *d.*: rubber tubing, *e.*: three-way stopcock, *f.*: "Record" syringe, *g.*: rubber tubing, *h.*: flask containing citrated blood, *i.*: blood-taking needle and tube, *j.*: tube for Higginson's syringe, *k.*: tube from thistle funnel.

seen). For this reason it is easily located in the infant, as one can confidently open the tissues down to the periosteum to find the vein lying on the bone.

Procedure.

After compatibility has been determined, usually by cross-typing, citrated blood is collected. At the Children's Hospital the blood is collected by the closed method, slightly modified from that described by Milroy and Matheson in THE MEDICAL JOURNAL OF AUSTRALIA. For purposes of giving blood to infants by transfusion by the method now described, collection of the blood in a beaker or any other container is quite satisfactory.

The infant's foot is bandaged to a splint and the position of the malleolar vein is noted, and under local anæsthesia a transverse or oblique incision is made across the line of the vein just proximal to the medial malleolus. By placing a pair of Spencer-Wells forceps in the wound and opening them in a plane at right angles to the incision, one can boldly open up the subcutaneous tissues as deep as the periosteum. When the periosteum is bared, the malleolar vein can be seen as a blue line upon the shining white surface of the bone. As a rule, a tourniquet is not required. The vein can then be mobilized with an aneurysm needle, and two pieces of catgut passed beneath it in the customary manner—a distal one for purposes of traction and a proximal one to tie the needle in the vein later on. With fine scissors the vein is then cut half across, and the needle and stilet are introduced in the manner described above.

Next, the "Record" syringe is attached to the stopcock, and the rubber tubing (*g*) connected to the flask of blood, as in Figure III, or dropped into the beaker of blood. The tap is adjusted and blood is drawn into the syringe. Then the tap is turned on, and any air in the syringe is expelled through the tube (*d*). As soon as blood is dropping from the adaptor in this tubing, the stilet is removed and the adaptor is fitted into the needle in the vein. The small amount of air in the needle can be ignored. The blood is then gently forced into the vein, and by refilling of the syringe and adjustment of the stopcock each time, the desired amount of blood can be given. When the transfusion is completed, the pieces of catgut surrounding the vein should be removed and a dressing applied. Rarely a horse-hair suture is required for the incision.

The amount of blood and the rate at which it is given depend upon the circumstances. In a very anæmic infant up to 66 cubic centimetres of blood per kilogram (one ounce per pound) of body weight can be given. Usually it is desirable to take at least from 20 to 30 minutes to give, say, 90 cubic centimetres (three ounces) of blood to an infant weighing 2·7 kilograms (six pounds).

In larger infants, it is more satisfactory to transfuse blood by the continuous drip method, but this is not always possible when the veins are small. The type of needle and stilet described above has been found so satisfactory for intravenous therapy that it is now used throughout this hospital for all blood transfusions and the intravenous administration of saline solution. A slightly larger needle than that described is used for continuous transfusion.

Summary.

What is regarded as a very reliable method of giving blood transfusions to infants is described.

Due attention must be paid to the anatomy of the malleolar vein, the use of a needle and stilet as cannula, and a means of introducing the blood at a pressure greater than gravity.

Reports of Cases.

THE REPAIR OF A FACIAL NERVE LESION BY A BALLANCE-DUEL GRAFT.

By G. A. D. McARTHUR, M.D.,

Honorary Surgeon to the Eye and Ear Hospital, Melbourne.

THE experimental work of the late Sir Charles Ballance and of Arthur B. Duel in the repair of facial nerve lesions has produced much improvement, both in the rate of recovery and in the final condition of the face after a palsy.

After much experimental work on monkeys, in which a portion of the facial nerve in the Fallopian canal was excised, it was found that recovery took place most quickly when a piece of prepared graft, in which Wallerian degeneration had occurred, was inserted in the gap between the cut ends. The graft was taken from the anterior femoral cutaneous nerve, which was severed and allowed to remain *in situ* for two or three weeks. During this time the axons and myelin sheaths underwent degeneration and were absorbed. The graft was then just a bundle of hollow tubes. When it was excised and placed in the gap between the cut ends of the facial nerve it was immediately ready to act as a conductor to the axons in the proximal segment. These quickly grew down the hollow tubes in the graft and then entered the hollow tubes in the distal segment of the facial nerve, down which they continued to grow till the end plates in the muscle were reached.

The facial palsy diminished much more quickly with the degenerated graft than when a fresh graft was used. In

FIGURE I.
Showing facial palsy after the mastoid operation.

this the axons had to degenerate and be absorbed before the axons from the proximal end could push down the tubes. Absorption took a long time when the graft was displaced into a new bed where the circulation was naturally of the poorest.

The end-results where a graft was used were much superior to those obtained when a nerve from the neck, such as the hypoglossal, was anastomosed with the distal segment. In these cases associated movements and twitchings apparently detracted to a certain extent from the good results.

The following is the clinical record of a patient who sustained an injury to the facial nerve on the right side during the course of a Schwartze mastoid operation. The injury was repaired by means of a degenerated nerve graft.

Clinical Record.

Miss M.G., aged thirty-two years, a subject of chronic nasal sinusitis and bronchiectasis, on December 20, 1936, underwent an operation for acute mastoiditis.

The mastoid process was found to be grossly pneumatized. One gallery of cells lay far forward under the posterior wall of the meatus and ran down to the most anterior part of the tip.

FIGURE II.
Condition one year after nerve graft.

Immediately after the operation, complete facial palsy was noticed on the right side, the side on which the operation was performed. A fortnight later the area of operation was explored. It was found that when the anterior gallery of cells was opened about one centimetre of the facial nerve had been removed, from the stylo-mastoid foramen upwards. The severed ends were easily identified. The anterior femoral cutaneous nerve was then exposed in the thigh, severed and marked for future identification. The Schwartze mastoid operation was turned into a radical operation to facilitate approach.

Five weeks later, on February 12, 1937, the operation area was again exposed and the cut ends were identified. This was more difficult than at the first exposure, owing to the growth of granulations. This especially applied

FIGURE III.
Condition one and a half years after nerve graft. It shows good closure of the eye.

to the distal segment. Its cut surface was freshened as much as possible. At the proximal end the Fallopian canal was further opened and a small portion of the nerve was cut off with a very sharp knife to freshen the end. The prepared graft was removed from the thigh and two pieces were laid side by side between the cut ends of the facial nerve. They were then covered with a piece of sterile tin foil, and gauze soaked in normal saline solution was used as a dressing. In the handling of the graft, Duel's

instructions were meticulously followed; that is, the nerve was held by the sheath and cut with the sharpest possible knife, so that the hollow tubes left by the degenerated axis cylinders would not be crushed.

The face was treated by massage and galvanism twice a week. No splint was worn to hold up the corner of the mouth. For a period of six months there was no improvement in the condition, the facial muscles remaining atonic and flaccid. By the seventh month some improvement began. The muscles felt more firm and the mouth did not droop so much. By the eighth month the mouth had a normal appearance in repose, and the patient noticed that food did not collect in the cheek so much as formerly. At the end of a year the tone in the face was so good that food no longer collected in the cheek during a meal. Movement was beginning to return and a faint smile could be produced (see Figure II). A year and a half after the operation the patient could close the eye, and the lids, which until then had been sutured, were released (Figures III and IV).

FIGURE IV.
Face in repose, one and a half years after operation.

Acknowledgements.

I am greatly indebted to my colleague, Dr. Mark Ashkenasy, for his skilled assistance during the operation, and to Nurse Smith, of the theatre staff of the Eye and Ear Hospital, for the photographs.

Bibliography.

A. B. Duel: "The Operative Treatment of Facial Palsy", *The British Medical Journal*, Volume II, December 8, 1934, page 1027.

Reviews.

HANDBOOK OF PRACTICAL BACTERIOLOGY.

MACKIE AND MCCARTNEY'S invaluable little book, known in former editions as "An Introduction to Practical Bacteriology", now appears in its fifth edition as a "Handbook of Practical Bacteriology",[1] expanded to such an extent that the original title is no longer adequate.

New knowledge, modifications in laboratory practice, and the introduction of new methods have necessitated a somewhat larger volume; but the book still remains a concise presentation of all the essentials of the bacteriological and serological technique required for the investigation of disease in the human subject.

In this *vade mecum* of laboratory workers, as we described it on a former occasion, the general arrangement of earlier editions is maintained, the subject-matter being treated in three sections. In the first, of an introductory nature, the biology of microorganisms is discussed and the fundamentals of immunology are presented. In the second section, which deals with bacteriological and serological technique, the reader finds himself in the very atmosphere of a work-a-day laboratory, and valuable practical points stand out from every paragraph. In the third section of the book the essential features of the pathogenic and commensal microorganisms are described, the last chapter being devoted to a brief statement of current views of viruses and the human and veterinary disease attributed to them.

We do not share the authors' enthusiasm for screw-capped bottles as vehicles for culture media, nor do we quite agree with the criteria they adopt in the virulence test in the rabbit for the differentiation of human and bovine tubercle bacilli. It is stated on page 351 that if rabbits are inoculated intravenously with 0·01 to 0·1 milligramme of dried tubercle bacilli of the bovine type, the animals usually die within two months. We would rather say within twenty-one days; and we should not be impressed with the virulence to the rabbit of a strain of tubercle bacilli that approached the time limit of two months before killing the animal.

Every phase of laboratory work is covered in a concisely practical manner, and the bench worker, when in difficulties, will be well advised to turn to his "Mackie and McCartney".

[1] "Handbook of Practical Bacteriology: A Guide to Bacteriological Laboratory Work", by T. J. Mackie, M.D., D.P.H., and J. E. McCartney, M.D., D.Sc.; Fifth Edition; 1938. Edinburgh: E. and S. Livingstone. Crown 8vo, pp. 597, with illustrations. Price: 12s. 6d. net.

TROPICAL NUTRITION AND DIETETICS.

So great has been the development in recent years of biochemical knowledge, particularly of those of its phases which relate to food or nutrition, that it has become virtually impossible for the average practitioner to follow recent developments in the literature. Any volume, therefore, that succeeds in presenting an up-to-date account of nutritional and dietetic principles, incorporating the most recent advances and placing them in a good perspective, is at once very useful and welcome. Such a book is Lucius Nicholl's recently published "Tropical Nutrition and Dietetics".[1] In it is given a clear, concise, and practical account of the relation of food to health and disease in the tropics. For some years Dr. Nicholls has been actively engaged in nutritional and other research into problems of tropical medicine. Throughout the book he makes a truly scientific approach to his subject, displays an essential respect for experimental facts and evinces a gratifying disinclination to accept statements inadequately proved by experiment.

The book is primarily intended for medical practitioners who work among the masses in the tropics. For them it should prove of great value, particularly in view of the scarcity of concise, authoritative information concerning dietetic requirements in hot climates. Its usefulness, however, is by no means confined to these workers, for not only is the larger section of the book devoted to an excellent account of current knowledge concerning the essential constituents of food, but there are also included useful chapters on dietary surveys, analysis of foods, surveys for nutritional defects and the prescribing of diets.

The author draws attention to the fact that, while diseases such as scurvy, beriberi and pellagra are extreme conditions due to dietary deficiencies, only in recent years has it been realized that manifestations of a less profound nature are prevalent in many tropical (and other) countries and are due to various shortages in the diets. Among the many advances being made at present, which open up fresh avenues for nutritional research, are the discoveries of tests for the early stages of avitaminosis in man—tests for vitamin *C* in urine as an indication of latent scurvy, the "bradycardia" method of determining clinical and subclinical deficiencies of vitamin *B*, and photometric methods for the examination of persons for the early stages of night blindness due to vitamin *A* deficiency. Practical descriptions of these tests are incorporated as appendices.

The book is essentially practical and will well repay the study of practitioners and others interested in nutrition.

[1] "Tropical Nutrition and Dietetics", by L. Nicholls, M.D., B.C., B.A.; 1938. London: Bailliere, Tindall and Cox. Demy 8vo, pp. 175, with illustrations. Price: 7s. 6d. net.

The Medical Journal of Australia

SATURDAY, DECEMBER 31, 1938.

All articles submitted for publication in this journal should be typed with double or treble spacing. Carbon copies should not be sent. Authors are requested to avoid the use of abbreviations and not to underline either words or phrases.

References to articles and books should be carefully checked. In a reference the following information should be given without abbreviation: Initials of author, surname of author, full title of article, name of journal, volume, full date (month, day and year), number of the first page of the article. If a reference is made to an abstract of a paper, the name of the original journal, together with that of the journal in which the abstract has appeared, should be given with full date in each instance.

Authors who are not accustomed to preparing drawings or photographic prints for reproduction, are invited to seek the advice of the Editor.

NEW YEAR'S EVE.

ANOTHER year has been left behind in Time's swift passage through the centuries. Time races; the strongest of us are hard put to it to keep pace with him, and many are left panting in the rear. The conventional figure of the thin, leisurely old gentleman dressed in a flowing robe and bearing a scythe and hourglass belongs to a past generation, if indeed it belongs to any generation. Time is a vigorous fellow, whose winged feet carry him through the years with merciless speed. Let us consider how we have fared in our contest with him during the lap of 1938.

Advancement of knowledge has continued, no less in medicine than in other sciences. Much attention has been paid to improvement in therapy, and it is here probably that the greatest progress has been made. But something more is required than the knowledge of how to achieve a certain therapeutic result; machinery must be provided for the practical application of such knowledge. In this respect the medical profession in Australia is liable to be hampered. Governments and other bodies do not always realize that money spent on the health of the community or in the saving of lives is money wisely invested, that it will bring a return of greater value than if it were invested in any other way. It is the profession's duty, not only to heal and protect the community, but also to convince the various governments that the most efficient methods of combating disease must be at hand. In many instances a government has merely to remove an obstacle to make these methods available. It is fitting that at this point we should mention the National Health and Medical Research Council. This new body has already carried out valuable work. We believe that it will have a great influence for good on the advancement of medical science in Australia.

National health insurance has been discussed in so many ways and inspected critically from so many aspects by so many people that it scarcely seems necessary to mention it here. We would merely repeat that in its present form it is not truly a health measure and that unless it were greatly modified Australia would be better off without it. If national health insurance as proposed for Australia is evidence of progress, then the medical profession in Australia has shown, what probably it has never shown before, that it is prepared to obstruct progress. Every logical person will admit that there is something wrong here.

There have been other interesting developments in our domestic affairs. Not the least interesting is the abandonment of the Queensland hospitals' honorary system. It seems a pity that this change should have been found necessary. The finest characteristic of our profession has been a readiness always to give free attention to the poor. But this is a mercenary age, and many will argue that a man should be paid for his many hours of arduous work in the public hospitals. We may sum up by saying that henceforth in the hospitals of the Brisbane and South Coast Hospitals Board, medical officers will be working for the Government instead of for the hospitals or the public hospital patients. We believe that the medical men may be relied on to do their duty whatever the conditions; but we could imagine happier relations than these.

The inaugural meeting of the Royal Australasian College of Physicians is further evidence that the profession in Australia has not stood still. The college will improve the standard of medicine in this country, if it does nothing more than stimulate men to increase their knowledge so that they may become eligible for admission to it. We welcome this college and hope that in the fullness of time it will develop the pleasing form of maturity and gather such traditions as will make it truly noble.

Australia is fortunate in being so far from the scenes of bloodshed and oppression in the Old World; but when the threat of war comes, as it did in September, 1938, we find that we are not so isolated after all. The Commonwealth Government has at last realized that Australia may be involved some day in another conflict. If such a day comes, the medical profession will not be found wanting, but will respond to the call for the legions of mercy as it did in the days of the glorious A.I.F.

In common with other countries that are willing to succour the oppressed and the weak, Australia is faced with the problem of what to do with the outcasts that are streaming from the countries of Nazism. We are concerned particularly with Jewish medical practitioners, graduates of foreign universities. Their plight is unfortunate; but, for the protection of the profession, and indeed the people of Australia, they cannot be allowed immediate registration. This is possible only if there are reciprocal arrangements with the country of their graduation. No other method would be workable. No doubt the men of ability, the men we shall welcome, will find little difficulty in surviving the several years before they can qualify for registration in their adopted country.

These are a few of the thoughts that come to us as we face the new year. Time, our relentless competitor, strides forward into 1939. Let us race with him. It is an exciting race, full of interest and alive with incident. Few have the fortune to lead in it at any stage; but all who have the will to win and who take pleasure in the contest can at least maintain their places in the van until the day comes when they can honourably retire. In 1939 let us not lag behind.

Current Comment.

ACCESSORY SPLEENS.

SUPPLEMENTARY or accessory spleens (*lienculi*) are not uncommon. They are generally small and globular and situated in the gastro-splenic omentum, usually attached to the gastro-splenic ligament near the hilum of the spleen. They are found less often in the great omentum. They are red in colour and similar in structure to the spleen. They vary in number from one to twenty, and their size ranges from that of a pea to that of a walnut.

R. F. Robertson has reviewed the subject of accessory spleens with a view to establishing their clinical importance.[1] He remarks that, in view of the frequency with which they are found at autopsy, it is strange that they are not more often encountered by the surgeon. One case has been reported in which 400 were found in various locations in the peritoneal cavity. This, however, is quite eclipsed by an instance in which 1,000 were found five years after a gunshot wound which involved the spleen itself. Different observers have estimated the frequency of their discovery at autopsies as ten or eleven *per centum*. Robertson, however, remarks that the distinction between genuine splenic substance and hæmolymph glands has not always been definitely established. He insists that an accessory spleen is an anomaly. Different authorities assign two causes for its presence—trauma and development. Beneke, quoted by E. Kaufmann, considers that trauma, with implantation and later regeneration of splenic particles, accounts for many accessory spleens. F. C. Helwig believes that intrauterine trauma may be the cause in many instances. He has recorded two cases of multiple spleens in which uterine trauma was evidenced. In each case the main spleen was divided into lobes by fibrous bands. In addition there were anomalous fibrous bands in the region of the liver and gall-bladder. The preponderance of opinion, however, favours the developmental theory as the most adequate explanation of many instances of accessory spleens. The end-result is merely a displacement of normal splenic tissue, but the time and conditions under which such changes occur are of importance in determining the final location of the accessory splenic substance. W. A. Sneath has recorded a remarkable case in which the accessory spleen was in the scrotum, attached firmly below to the upper pole of the testis and to a tail of spleen above by a fibrous band, which ran from the inner aspect of the spleen across the peritoneal cavity and down the left side to the left internal abdominal ring. Here it joined the spermatic cord and, passing through the inguinal canal, ended in a bulbous portion that adhered to the upper pole of the testis.

The left testis in its original position, as explained by Robertson, lies close to the spleen. But propinquity alone does not adequately account for the occurrence of accessory spleens. The spleen

[1] *The Canadian Medical Association Journal*, September, 1938.

is developed in the dorsal mesogastrium of the embryo and first appears as a localized growth in the mesoderm of the mesogastrium at the beginning of the fifth week of fœtal life. At this time the growth of the lung buds is forcing the stomach from its cervical position towards the caudal extremity and the stomach takes up its position (with the mesogastrium) level with the lower thoracic segments. At this time also the ridge on the inner end of the Wolffian body, from the hinder part of which the testis develops, extends from the ninth to the twelfth thoracic segment. The primitive genital gland lies in the iliac fossa. A. Keith remarks that in the lower mammals the splenic formation spreads caudally, even into the mesentery of the hind-gut, to form the "colic lobe". In the human subject a persistence of this condition explains the recorded presence of accessory spleens in the pouch of Douglas. The disappearance of the mesorectum would leave them stranded at that site. A localized extension to the left of this caudal prolongation of splenic tissue could come into close relationship with the adjacent testis which is in process of development. Such a relationship might extend to include a secondary vascular connexion, the vessels acting as a suspensory ligament and assuring the migration of the localized extension. Accessory spleens have frequently been found associated with other congenital abnormalities, for example, transposition of viscera. Warthin and Mayo have asserted that when the main spleen is both structurally and functionally defective, there is compensatory hyperplasia of accessory splenic tissue. Such tissue must have been misplaced before hyperplasia could occur.

Robertson reminds us that the pancreas arises from two or three separate *Anlagen*—one dorsal and one or two ventral. The dorsal one arises as a ridge-like evagination from the gut cephalad to the level of the liver. The mass of cells grows into the dorsal mesogastrium and becomes constricted from the parent epithelium except for a neck, which becomes the duct of Santorini. One or two ventral diverticula appear, of which one forms the duct of Wirsung. The smaller ventral pancreas grows to the right and dorsally and fuses with the dorsal head in the eighth week. In development a small amount of splenic tissue may become encapsulated in the pancreatic tissue. The occurrence of an accessory spleen in the body and tail of the pancreas is much more likely from a developmental standpoint than the formation of one in the head of that organ, and this is what actually happens. The clinical importance of accessory spleens has not up to the present received adequate recognition. Robertson states that accessory spleens account for some obscure pains and actual tumour masses in the abdomen. They have even been mistaken for a hernial sac or a supplementary testis. They may offer an interesting explanation for the unsatisfactory results obtained in the efforts to cure thrombocytopenic purpura by splenectomy. It would accordingly seem that an accessory spleen is not only splenic in structure but also in function.

British Medical Association News.

SCIENTIFIC.

A MEETING of the New South Wales Branch of the British Medical Association was held at the Robert H. Todd Assembly Hall, British Medical Association House, 135, Macquarie Street, Sydney, on October 27, 1938, DR. B. T. EDYE, the President, in the chair.

Sulphanilamide.

DR. E. B. DURIE read a paper entitled "Sulphanilamide" (see page 1103).

DR. J. N. CHESTERMAN read a paper entitled "The Use of Sulphanilamide in Some Clinical Conditions" (see page 1110).

DR. R. LEMBERG said that in opening the discussion he would limit himself mainly to one aspect of the many problems connected with the application of sulphanilamide, namely, its toxic effects. With regard to the mode of action, no more could be said than what Dr. Durie had brought forward. Only when much more was known about the biochemical processes in the bacterial cell would it be possible to deal adequately with problems of this kind.

Dr. Lemberg said that it was almost two years since, through the kindness of Dr. Durie, he had received a sample of blood from a cyanosed patient treated with sulphanilamide. In this blood he had established the presence of sulphæmoglobin; at that time its occurrence after treatment with the drug had not been described. He believed that the cyanosis was always due to the formation of either sulphæmoglobin or methæmoglobin; at least, he had never failed to discover one of these substances in the blood of patients who became cyanosed under sulphanilamide treatment, and he had observed small amounts of these substances occasionally even in the blood of patients without evident cyanosis. The paper of Marshall and Walzyl and other similar papers were open to criticism. Marshall and Walzyl stated that the oxygen capacity of the dark blood of cyanosed patients corresponded to the total iron content of the blood. Dr. Lemberg doubted whether this could be correct, in view of the fact that even in normal blood the oxygen capacity was significantly (about 5%) lower than would correspond to the total iron content, owing to the presence of non-hæmoglobin-iron in the blood. Since sulphæmoglobin combined with carbon monoxide, the determination of the carbon monoxide capacity could not indicate whether it was present or not.

What was sulphæmoglobin and how was it formed? One thing was certain: it was not the sulphur of the drug which entered the hæmoglobin molecule. Abuse of phenacetin, a sulphur-free compound, produced sulphæmoglobinæmia as well. It was not even established that sulphæmoglobin contained sulphur. Until that time, certainly, it had been obtained only *in vitro* by the action of hydrogen sulphide on hæmoglobin. Keilin had shown that sulphæmoglobin was not a compound of hæmoglobin with hydrogen sulphide, and that oxygen was necessary for its formation. Dr. Lemberg did not believe that Keilin's assumption that it was a compound of hæmoglobin and colloidal sulphur was acceptable. In the Kolling Institute of Medical Research at the Royal North Shore Hospital they had obtained compounds similar to, though different from, sulphæmoglobin, by the action of ascorbic acid and atmospheric oxygen on hæmoglobin. These compounds had as a prosthetic group no longer hæmatin, but bile-pigment-iron, the porphyrin ring having undergone an oxidative scission. They were intermediate products in the hæmoglobin breakdown to bile pigment. Sulphæmoglobin had three properties in common with these compounds: it had a similar absorption spectrum, its iron was more easily detached than that of hæmoglobin, and on splitting under certain conditions it yielded bile pigments. From similar experiments Professor Barkan, of Tartu, Esthonia,

had concluded that sulphæmoglobin was a bile-pigment-hæmoglobin. Although it was certain that prolonged action of hydrogen sulphide and air on hæmoglobin led to the formation of such compounds, it was not yet certain whether sulphæmoglobin itself belonged to this class. At least it was possible to confirm earlier observations that sulphæmoglobin could be reconverted into hæmochromogen; and it was somewhat difficult, though not impossible, to assume that the porphyrin ring in sulphæmoglobin was opened in a reversible way.

If Barkan's assumption was correct, it was not the sulphur of the hydrogen sulphide, but its hydrogen, that was active in the formation of sulphæmoglobin, hydrogen sulphide acting as a hydrogen donator, like ascorbic acid. Methæmoglobin arose under similar conditions, and the methæmoglobin cyanosis was to be considered as an initial stage of the sulphæmoglobin cyanosis. For this reason, and because sulphæmoglobin formation was an irreversible destruction of the blood pigment, while methæmoglobin could be reduced back *in vivo*, the cyanosis due to sulphæmoglobin had to be considered as the graver disturbance. It was easy to distinguish between the two compounds with a spectroscopic test. At the Royal North Shore Hospital the blood of patients under sulphanilamide or "Prontosil" treatment was tested for sulphæmoglobin as a routine measure.

If sulphæmoglobin arose in the way described, there were still some problems to be solved. It was unlikely that the drug acted as a hydrogen donator. It might act as a catalyst, like phenylhydrazine, which strongly catalyzed sulphæmoglobin formation *in vitro*. Until that time, however, they had been unable to establish such an action of the drug. Since only some patients displayed sensitivity, the drug might in the metabolism of these patients undergo transformation into a dangerous catalyst of sulphæmoglobin formation.

Dr. Lemberg went on to say that the disturbing action of sulphanilamide on the blood pigment metabolism was also evident from the increase of coproporphyrin excretion in the urine that it caused. Of 59 patients treated with rather small doses of the drug (about three grammes per day) at the Royal North Shore Hospital, only two showed small traces of sulphæmoglobin in the blood; but in no less than 19 cases the daily porphyrin excretion was abnormally increased, being as much as 110 to 650 microgrammes per day. Normal excretion was from 30 to 80 microgrammes per day. There could be little doubt that the light dermatitis that Dr. Durie had mentioned was due to the porphyrin. Patients under sulphanilamide treatment should, therefore, not be allowed to remain ambulant, unless an investigation of their urine had shown that the porphyrin content was normal. An exact determination of the porphyrin content of the urine was possible only where a spectrophotometer or spectrocolorimeter was available; but a method sufficiently exact to establish a considerable increase in porphyrin excretion with a hand spectroscope could easily be devised.

In conclusion Dr. Lemberg said that he would like to comment upon a point in the historical review given by Dr. Durie. The ingenious conception of Ehrlich had had to come first; but after this it was not the investigation of a worker who set out to discover an antidote against streptococcal infection, but blind laborious work in a field not at all connected with that of therapeutic problems which led to the success. This showed the essential unity of science. It was the clever and successful policy of a German firm of chemists to have each field thoroughly skimmed by a large number of scientifically trained investigators, whose scrutiny even side issues did not escape. This method might appear wasteful, but in the long run the methodical approach secured great successes, and one success covered the cost of many failures. To solve small problems a direct approach on specialized lines was often possible; but great problems could be solved only by investigations on a very broad basis and by coordinated effort.

PROFESSOR J. C. WINDEYER said that gratitude was due to the workers at the Women's Hospital, Crown Street, for the long and arduous work that they had done on the use of sulphanilamide. He hoped that more results would follow. A little more than two years earlier he had been in London with Leonard Colebrook. Colebrook was experimenting with mice, inoculating them with one hundred minimum lethal doses of hæmolytic streptococci. When he injected them with "Prontosil" he obtained 100% of cures; when he did not inject them with "Prontosil" he obtained a mortality of 100%. Professor Windeyer had remarked then that it looked as though the infectious wards at the obstetric hospitals could be closed. Colebrook had disagreed with this view, and he had been correct in his disagreement, for, although these drugs killed certain types of hæmolytic streptococci, they would not kill all organisms in the blood. That stage seemed to be coming. The clinical aspect of puerperal infection was of interest. Some eleven years earlier, as Bancroft orator in Brisbane, Professor Windeyer had talked about puerperal septicæmia and post-abortional septicæmia, and had mentioned that there were clinical differences between them. In septicæmia after abortion the mortality rate was 86%; the mortality rate in septicæmia after labour was 57%. In septicæmia after abortion death occurred in 64% of cases within 14 days; in septicæmia after labour death occurred in only 34% of cases within 14 days. After abortion peritonitis was common; after labour phlegmasia and pyæmia, which followed uterine thrombophlebitis, were common complications. These observations indicated that the infecting organisms were different. The hæmolytic streptococcus was the common infecting agent after abortion, while in infection after labour an anaerobic streptococcus was more likely to be found. The sulphanilamide group of drugs had more effect on hæmolytic streptococci; the results of its use should therefore be better after abortion than after labour. At the Royal Hospital for Women the results of treatment with sulphanilamide, in a comparatively small number of cases, seemed to indicate a greater reduction in the mortality rate after abortion than in that after labour. It had been suggested that during the last few years streptococcal infection had become less common or less virulent. It was difficult to prove whether this statement was true or not. Professor Windeyer said that he had collected figures from the records of the septic block at the Royal Hospital for Women, which he would quote. The figures referred to all patients admitted suffering from all types of infections of the genital organs after labour or abortion, or from breast abscesses. During the period from 1934 to 1936 there had been 848 admissions with 52 deaths, a mortality rate of 6·2%. Professor Windeyer said that he thought that Dr. Chesterman had in his paper made a mistake about the mortality rate from puerperal infections, which he had stated to be 70%; he must have meant the mortality rate from puerperal septicæmia. During the period from the beginning of 1937 until the time of the meeting there had been admitted to the infectious ward of the Royal Hospital for Women 624 patients, 19 of whom had died, the mortality rate being 3·2%. This was approximately half the mortality rate during the period from 1934 to 1936. The main improvement in treatment was the use of sulphanilamide, although other slight alterations had been made. At the Royal Hospital for Women, in septicæmia due to all types of streptococci the mortality rate was 50%, and in that due to hæmolytic streptococci it was 40%. These figures were substantially the same as those at the Women's Hospital, Crown Street.

DR. A. J. GIBSON thanked the speakers for their papers. He said that he thought the Women's Hospital, Crown Street, very fortunate to have two such keen workers as Dr. Durie and Dr. Chesterman. Dr. Chesterman had been particularly interested in this form of treatment ever since its introduction to Australia. They had tried the new treatment at the Women's Hospital soon after its introduction. They had been fortunate in securing a large quantity of the drug when it first came to Sydney. It had been decided that the drug should be used very accurately, and should be used only in proved streptococcal infections. It was realized that if each member of the honorary staff investigated these cases himself no one would have many to deal with. It was

therefore decided that Dr. Chesterman should be allowed to deal with every case of septicæmia and work in collaboration with the attendant practitioner. As a result, a few points of importance about the drug had been elicited. The main one was that every patient with an elevation of temperature during the puerperium should have an accurate bacteriological examination at the earliest possible moment. If streptococcal septicæmia was recognized early and if treatment with sulphanilamide was instituted straight away, the patient had a better chance of recovery. In the early days they had always made a bacteriological examination before giving "Prontosil", in order to classify the infecting organism. Now in these cases they gave sulphanilamide straight away and at once took a cervical swabbing. If no hæmolytic streptococci were found, then the administration of sulphanilamide could be stopped forthwith. The small initial dose was useful. At the Women's Hospital it had been very interesting to notice the response to sulphanilamide therapy in pyelitis. In one case, in which the urine had contained 150 to 200 pus cells per high-power field of the microscope, the number dropped to one or two pus cells per field in four days, the temperature became normal and the patient's condition was good. She was still harbouring *Bacillus coli communis*, but she was much better.

PROFESSOR H. K. WARD praised the standard of the papers and the clear way in which the subject had been presented. He said that he had very little to add to Dr. Durie's description of the mode of action of sulphanilamide. He thought it surprising that the world had had to wait for so long for an efficient therapeutic drug in infectious diseases. It appeared that medical men had been too impatient and had not had sufficient faith in the body's faculty of dealing with its parasites. They had been too obsessed with the test tube and wanted some dramatic effect. They had been seeking a bactericidal drug rather than a bacteriostatic drug, and they had paid too little attention to what was going on in the body. They should look on infectious disease as more in the nature of a balance between the rate of multiplication of the parasite and the rate of its destruction by the host. All that the sulphanilamide drugs did was to swing the balance in favour of the host by slowing down the rate of reproduction of the parasite. Interesting and good work had been done on gonorrhœa at Saint Mary's Hospital, where it had been shown that if treatment with sulphanilamide was instituted at the beginning of the disease the effect was not so good as if its administration was delayed for ten days. The reason was bound up with the fact that the human body had, as was known, no antibodies to the gonococcus. The delay of ten days provided time for the formation of antibodies, which aided the slowing-down action of the drug. Professor Ward said that Dr. S. A. Smith had asked him to refer to the new product "M. and B. 693". It had been tried in the treatment of patients with pneumonia at the Prince Henry Hospital, and while the results had been promising, no definite statement could be made at that stage.

DR. B. T. EDYE, from the chair, said that one of the most interesting features of the meeting was that results had been given of painstaking work carried on over a number of years, work in which the profession had taken an active part. As a result a very useful drug, or collection of drugs, had been evolved. Dr. Edye pointed out that such a method of investigation would be ideal when new drugs were introduced, especially when exaggerated or incorrect claims were made. Frequently new drugs were put before the profession, accompanied by extravagant statements of their effects. Medical men often tried such drugs; but it took a considerable time to satisfy themselves that such drugs were valueless, and in the meantime the manufacturers had made substantial profits. There were always many drugs and preparations before the profession about which authentic information was unobtainable. There should be a method by which the profession could investigate them before they were allowed to be used. The speakers had taught those present a valuable lesson, by showing that such an investigation could be made.

Dr. Chesterman, in reply, thanked the other speakers for their comments, and said that he had only one thing to say. Professor Windeyer had thought that he had given 70% as the mortality rate of hæmolytic streptococcal puerperal infections. Dr. Chesterman had apparently not made it clear that what he had intended to convey was that of all deaths from puerperal infection, in 70% of cases the hæmolytic streptococcus was the causal organism.

ANNUAL GOLF COMPETITION CONDUCTED BY THE NEW SOUTH WALES BRANCH.

THE annual competition for the British Medical Association Golf Cup, presented by Dr. H. C. Rutherford Darling, was held at the Concord Golf Club on Thursday, December 1, 1938. Forty-six players competed. The competition, a stroke handicap, was won by Dr. W. P. MacCallum (handicap −18), with a score of 64, net.

Despite the time of the year, the weather fortunately was cool, thus helping to make the event the more enjoyable. It is expected that arrangements will be made in 1939 to have the event played off earlier in the year, during the cooler weather, when it is hoped that a larger number of members will participate and the occasion be even more successful.

The scores of the nine leading players in the 1938 competition were as follows: Dr. W. P. MacCallum—82 (18), 64; Dr. A. M. Ping—82 (17), 65; Dr. R. B. Holliday—87 (22), 65; Dr. K. M. Whiting—82 (16), 66; Dr. C. E. Vickery—91 (24), 67; Dr. C. Burns—84 (15), 69; Dr. R. Honner—87 (18), 69; Dr. F. C. Florance—81 (12), 69; Dr. V. Rich—89 (20), 69.

NOMINATIONS AND ELECTIONS.

THE undermentioned have been elected members of the Victorian Branch of the British Medical Association:

Alpins, Oscar, M.D. (Bologna), 109, Collins Street, Melbourne, C.1.

Kaw, Julian Frederick William, M.B., B.S., 1936 (Univ. Melbourne), 128, Riversdale Road, Hawthorn, E.2.

Smith, Herbert, M.B., B.S., 1937 (Univ. Melbourne), Mooroopna Base Hospital, Mooroopna.

Stevens, Frank Richard Tod, M.B., B.S., 1937 (Univ. Melbourne), 216, Auburn Road, Auburn, E.2.

Medical Societies.

MELBOURNE PÆDIATRIC SOCIETY.

A MEETING of the Melbourne Pædiatric Society was held at the Children's Hospital, Carlton, Melbourne, on August 18, 1938, DR. COLIN MACDONALD, the President, in the chair.

The Treatment of Hæmorrhage of the New-Born.

DR. IAN WOOD showed a male baby, aged three weeks, suffering from hæmorrhage of the new-born. The baby had been born at term, and the birth weight was 3·6 kilograms (eight pounds). Progress had been satisfactory until the seventh day, when he had vomited several ounces of coffee-ground material, and later blood had appeared in the stools. When admitted to the Children's Hospital, on the seventh day, the baby was extremely pale. The hæmoglobin value was 28% (Sahli); the remainder of the blood examination gave information typical of anæmia due to acute hæmorrhage.

A blood transfusion of 120 cubic centimetres (four ounces) was given into the internal saphenous vein of the ankle by means of the technique described by Dr. V. L.

Collins. By this means the hæmoglobin value was elevated to 75%, and the baby had an excellent colour and was vivacious and hungry. Three days later another transfusion of 90 cubic centimetres (three ounces) was given, as the hæmoglobin value had fallen to 55%. Thereafter there was no sign of hæmorrhage.

In discussing the problem of the treatment of hæmorrhage of the new-born, Dr. Wood emphasized the importance of a close study of the hæmoglobin level by means of an accurate hæmoglobinometer, such as the Sahli model. He said that this instrument was relatively cheap and very simple to use. If the hæmoglobin value remained above 60% it was probably safe to treat these infants by means of liberal feedings, preferably of breast milk, and by intramuscular injections of substances such as maternal whole blood (five cubic centimetres being given intramuscularly every twelve hours), "Clauden" or hæmostatic serum. The necessity for the maintenance of an adequate intake of food and fluid in these infants was usually not realized. Even if the hæmorrhage occurred in the stomach, no benefit was obtained by keeping the stomach empty. Mülengracht had shown that in the case of adults suffering from massive hæmorrhage due to peptic ulcer the best results were obtained by supplying the stomach with liberal quantities of food and fluid. In the case of the severely exsanguinated, drowsy infant, it was sometimes necessary to supply the milk by means of a stomach tube. A fine catheter was useful as a tube. It was best passed through the mouth and not through the nose, as the nasal passages were narrow and delicate. This procedure was rapid and simple, and caused no distress to the baby. If vomiting due to the irritant effect of the blood on the gastric mucous membrane occurred, it was wise to give small, frequent feeds.

In considering the necessity for transfusion one should be guided by the appearance of the infant, the frequency of the hæmorrhages, and the hæmoglobin value. A hæmoglobin level below 60% should be regarded as an indication for transfusion. The hæmoglobin level was the most informative of the various signs. If a transfusion was given, it was safe to elevate the hæmoglobin to a level above 80%, even from a level as low as 25%—a condition barely compatible with life. From 15 to 22 cubic centimetres (one-half to three-quarters of an ounce) of blood could be given per pound of body weight. Dr. Wood said that this calculation was a useful guide to the amount of blood required by exsanguinated infants. This could be administered in from half an hour to one hour, without any obvious impairment to the circulation. After adequate blood transfusion it was rare for the hæmorrhage to recur, for the blood not only removed the acute anoxæmia, but had a hæmostatic effect.

In conclusion, Dr. Wood said that if these principles were carried out the mortality rate would be greatly reduced. At the present time the commonest cause of death was delay in administration of the blood transfusion. During the past year he had seen at least four infants who were deathly pale and semi-comatose, and the estimation of whose hæmoglobin had revealed a level of below 30%. On the other hand, more than half the infants with hæmorrhage of the new-born recovered without receiving blood transfusion. Lightwood, of London, had shown that there was a natural tendency to remission, even if no treatment was given. Accurate hæmoglobin estimations and a liberal supply of milk would save many lives.

DR. V. L. COLLINS read a paper entitled "A Method of Giving Blood Transfusions to Infants" (see page 1121).

The Anatomical Basis of Chronic Pyuria.

DR. ERIC PRICE showed a series of X ray films illustrating the anatomical basis of chronic pyuria. The first related to a child, aged nine and a half years, who had been first seen by Dr. Price on November 9, 1935. The child had had intermittent attacks of pyelitis since babyhood. Various investigations were carried out. An excretion pyelogram was made, and revealed bilateral hydronephrosis and hydroureter, the left renal pelvis being disproportionately large. Retrograde pyelography was performed. Both ureteric orifices were seen to be gaping and patulous. The bladder was otherwise normal. The pyelogram confirmed the presence of dilatation, but revealed in addition a constriction at the pelvi-ureteric junction. Cystography revealed a vesico-ureteric reflux. This enabled the obstruction at the pelvi-ureteric junction to be confirmed. Examination of the urine revealed gross pyuria and the presence of *Bacilli coli communis*.

A diagnosis of aberrant artery on the left side in addition to the general dilatation was therefore made, and was confirmed at operation. Pyeloplasty, by means of excision of a diamond-shaped portion, was performed. The operation was shown in a later pyelogram to have improved the pelvic aspect of the hydronephrosis. This, however, merely revealed the gross renal hydronephrosis, and the result was disappointing. Nephrectomy was avoided because of the bilateral nature of the lesion.

The second X ray film shown by Dr. Price related to a child, aged six years, whom he had first seen on August 24, 1935. The child had had an attack of acute pyelitis.

Excretion urography and retrograde pyelography had shown the left side to be normal. On the right side the ureter and pelvis were bifid. The upper pelvis seemed to consist of only one calyx. Dr. Price said that since that time the child had had no symptoms until recently, although whenever it was examined the urine contained a few pus cells. In the month preceding the meeting she had had a slight recurrence of symptoms.

The next patient of whom Dr. Price showed X ray films was a girl, aged four years. She had first been seen by Dr. Price on March 22, 1938, with a history of recurrent attacks of pyelitis since the age of nine months. She was not having an attack when examined. The urine contained a few pus cells and *Bacilli coli communis*. Excretion pyelograms were inconclusive. A cystoscopic examination was made and the bladder and left ureteric orifice were found to be normal, while on the right side two ureteric openings were seen of otherwise normal appearance. All three ureters were catheterized, but the pyelograms revealed nothing beyond the double ureter. The lower ureter drained the upper pelvis, the excretion from which was delayed.

Dr. Price next showed X ray films relating to a girl, aged thirteen and a half years. She had been treated between February, 1934, and July, 1937, for low-grade infective polyarthritis. Infected teeth and tonsils had been removed without benefit, and further examination had revealed a mild symptomless pyuria. A complete urinary investigation was undertaken. This revealed a right pelvic hydronephrosis and hydroureter of mild degree, with some delay in excretion of the dye. The ureteric orifice was inflamed and patulous. The left kidney, ureter and bladder were normal. Dr. Price said that since July, 1937, there had been no arthritic or urinary symptoms, and she had been very well, though the urine always contained a little pus. In January, 1938, pyelography showed that the dilatation had not varied. In May, 1938, presacral neurectomy was performed. An excretion pyelogram taken a fortnight later showed a return to practical normality.

Dr. Price remarked that the value of this case was to a large extent spoiled by the retrospective discovery of an indefinite filling defect in the lower end of the right ureter. It might have been a uric acid calculus, or it might not. On this point it might be said that at operation the right ureter was seen to be twice the diameter of the left.

Dr. Price went on to say that the anatomical abnormalities of the urinary tract commonly met with in chronic pyuria fell into two groups. The first group consisted of dilatations. These might affect the pelvis only, the pelvis and ureter, with or without a normal ureteric orifice, both pelves and ureters or the bladder. They might also be associated with megacolon or Hirschsprung's disease, though this association was rare. The cause in this group might be neuromuscular or mechanical. A primary neuromuscular defect seemed to explain most cases. The nervous control was by no means understood; but it seemed that there might be a failure of the parasympathetic detrusor mechanism, or an overaction of the sympathetic. This resulted, not so much in a passive dilatation as in achalasia, but in an active relaxation. Dr. Price remarked that this might be the reason for the apparent success in the case of the girl aged thirteen and a half years.

Occasionally mechanical artery factors might become important. The most usual was the aberrant artery, but other factors might cause obstruction at the pelvi-ureteric

orifice, such as valvular openings of the ureter or an ectopic origin of the ureter from some point other than the lowest point of the pelvis. Probably these mechanical lesions were not primary, but as the hydronephrotic sac became enlarged from some other cause they provided a secondary obstructive factor.

Clinically the cases could be arranged in four groups: (i) renal tumour, most frequently met with in infants; (ii) abdominal colic, the usual symptom in young adults; (iii) chronic or recurrent pyelonephritis, the common story in children; (iv) silent cases, discovered accidentally, in which probably very little infection was present.

Dr. Price said that the second group of chronic abnormalities of the urinary tract consisted of duplication of the ureters. They might be bifid or double to the bladder, or rarely, might open ectopically into the urethra. The last condition was a rare cause of incontinence. It was difficult to imagine why duplication should predispose to chronic infection. One might conjecture that with the congenital defect there was associated a neuro-muscular defect interfering with the free passage of urine.

Other causes of chronic pyuria included calculus and tuberculosis. Calculi were especially likely to occur with long recumbency when the patient was receiving a diet rich in calcium. Such cases not infrequently occurred at the Children's Hospital, Frankston. Dr. Price said that when a careful search was made many patients with bone and joint tuberculosis were found to have slight pyuria and tuberculous bacilluria. This appeared to be due to a subclinical lesion in the kidney parenchyma and to be of good prognosis. While the great majority of patients with mild or severe urinary infection did not require operation, it would appear essential that in all such cases a complete urological examination should be made. This should include cystoscopy and retrograde pyelography as well as excretion pyelography, since each of these methods might disclose a lesion not revealed by the other. In addition the lesion had to be localized and lateralized. It might be that only one kidney, or one portion of a bifid kidney, was diseased. It could not yet be stated that conservative surgical treatment was on a sure footing; but only in the early cases was it possible to expect a satisfactory result. By the time that the whole urinary tree was infected, or that dilatation had become permanent by reason of structural changes in the walls of the pelvis and ureter, or by the reduction of the kidney to a functionless bag of pus, it was not reasonable to expect a cure by removal of the primary cause.

Talipes.

DR. WILFRED FORSTER showed a series of patients to illustrate the varieties of talipes and the different stages of their management. He also discussed the main principles of management.

DR. B. KEON-COHEN stated that he had seen a number of patients in England treated by means of the Dennis-Brown type of splint. He had been interested in the modification of this splint that had been used. In the ordinary type of talipes, in which the foot and heel were long, it was easy to fit this type of splint and a good result was obtained; but in cases of talipes in which equinus and varus deformities were present and the heel was small, he could not see how the Dennis-Brown splint could be fitted satisfactorily. Strapping and splinting appeared satisfactory in these cases. He disagreed with the principles of vigorous manipulation, for he felt that the essential part of the treatment was the gradual moulding of the foot. There should be no jerking movements, and the calcaneo-cuboid joint should be supported all the time. In the early stages he had found the most satisfactory response was obtained by manipulation and strapping repeated every week. Later, when a good position had been obtained, the Dennis-Brown splint was very useful for its maintenance.

DR. E. E. PRICE agreed that the type of patient with the long foot and good heel was easily managed with strapping, but thought that it did not make much difference whether strapping was placed above the knee or not. At a later date, when the patient was stronger and wanted to put his feet to the ground, the chief difficulty was in the maintenance of the position. Dr. Price's practice was to use shoes when the patient was desirous of walking. He thought that the use of the splint as described was an excellent method; he was interested in its application to the treatment of *metatarsus varus*.

DR. H. DOUGLAS STEPHENS said that the type of talipes in which the foot and heel were small was always difficult. He could not see that this method of treatment offered any distinct advantages. He mentioned also the dangers of powerful manipulation in the early stages, and pointed out the possibility of a fractured fibula and ulcerated skin on the medial side of the foot. Sir Robert Jones had been quite content to obtain reduction in from two to three months.

Tuberculosis in Childhood.

DR. REGINALD WEBSTER discussed some aspects of tuberculosis in childhood. He said that during the past few months he had been engaged in the cultivation of tubercle bacilli from as many sources as possible, other than pulmonary sources. In the course of this work he had had considerable success in the cultivation of tubercle bacilli from the cerebro-spinal fluid and the urine. As a result he had become particularly interested in the question of tuberculous meningitis, and in that of renal tuberculosis and the degree of probability attaching to the conception of tuberculous bacilluria without renal lesions.

Since January, 1938, seven children had died in the Children's Hospital of tuberculous meningitis. From the cerebro-spinal fluid of each of them he had cultivated the tubercle bacillus. This had prompted a revival of interest in a condition which for some years he had regarded as not very attractive pathologically, because its pathogenesis seemed well established and indeed obvious.

Research of recent years, however, had shown that the last word had not been said regarding the origin of tuberculous meningitis, and that the simple conception of a direct hæmatogenous sowing of the pia-arachnoid with tubercle bacilli as but a phase in the tuberculous bacillæmia of miliary tuberculosis, stood in need of critical examination and revision.

The first workers to challenge the conventional view of direct hæmatogenous infection as precipitating tuberculous meningitis were Rich and McCordock, whose work appeared in *The Bulletin of the Johns Hopkins Hospital* in 1933. As circumstances that impaired the validity of the established idea, Rich and McCordock cited the observations: (i) that meningitis might be absent in the most extreme cases of miliary tuberculosis; and (ii) conversely, there were many cases in which meningitis occurred in the complete absence of miliary tuberculosis.

Dr. Webster said that the second statement might be allowed to stand with reference to adults, but he could not accept it as applicable to young children. It was an extremely rare event to find tuberculous meningitis in children apart from some degree of miliary tuberculosis in the thoracic and abdominal viscera.

It was, indeed, a fully substantiated experimental fact that the injection of even massive doses of tubercle bacilli into the blood stream of animals, while causing severe generalized miliary tuberculosis, did not produce simultaneous acute exudative meningitis, not even when actual emboli of bacilli were introduced directly into the carotid artery. The immediate effect of such injections was the production only of rare, discrete tubercles in the meninges. In the subsequent evolution of such tubercles, by caseating and softening they might discharge into the subarachnoid space and initiate the familiar exudative tuberculous meningitis; but this meningitis was never in direct and immediate relation to the intravascular injection.

The general tenor of the thesis of Rich and McCordock was that tuberculous meningitis had its origin in the discharge of bacilli into the cerebro-spinal fluid from adjacent, older, caseous tuberculous foci. They found by careful search in the substance of the brain or cord, in the meninges, in the bones enclosing the central nervous system, in the ependyma of the ventricles or the chorioid plexus, such discharging foci in 77 of 82 cases of tuberculous meningitis which they investigated.

Rich and McCordock insisted that the search for such foci must be meticulously thorough, and thought that they might easily be overlooked by other observers. Nothing less than the careful examination of serial sections of the brain, not more than three millimetres in thickness, aided by transillumination of the thin slices, constituted an adequate search.

Dr. Webster said that he had examined the brains of three children who had died of tuberculous meningitis, and had four others put away to subject to a scrutiny as opportunity arose. As yet he had not been able to find discharging foci abutting on the meninges, but he would offer no criticism on that ground. In the ultimate analysis tuberculous meningitis would have to be attributed to hæmatogenous infection, for how else could the discrete discharging foci described by Rich and McCordock arise? Their essential point was that the onset of diffuse meningitis was contingent upon the fortuitous development of such foci, and not upon the mere presence of large numbers of bacilli in the blood stream.

The consistent failure of animal experiment to produce meningitis by the inoculation of tubercle bacilli into the blood stream seemed to support strongly the conclusions reached by Rich and McCordock; but their findings had not been universally accepted, and during the past two years further attempts had been made to arrive at the facts. An annotation in *The Lancet*, of January 15, 1938, quoted the findings of A. B. Ragins. As the result of an examination of 47 brains he concluded that in 38 of them the evidence did not bear out the contention of Rich and McCordock, but pointed to direct hæmatogenous spread. C. Radmann, in a much smaller study, concluded that meningitis occurred both with and without the previous formation of solitary tubercles.

In order to try to clarify the situation, A. R. MacGregor and C. A. Green, of Edinburgh, whose work was published in *The Journal of Pathology and Bacteriology*, undertook a minute and comprehensive study of 112 brains. In general the result of their work led the Edinburgh workers to support the view of Rich and McCordock; but they recognized that this view did not account for the close association found between miliary tuberculosis and tuberculous meningitis.

Dr. Webster remarked that it was particularly in infants and young children that tuberculous meningitis and miliary tuberculosis were so frequently, he might almost say invariably, associated. If it were granted that the meningitis arose by infection from contiguous discharging foci, was the presence of miliary tuberculosis in over 90% of the cases of tuberculous meningitis in infants and young children to be attributed to nothing more convincing than coincidence? He had read the explanation advanced by Rich and McCordock of what they termed the "unquestioned frequency of the coincidence of tuberculous meningitis with miliary tuberculosis" in infants and young children, but he could not go all the way with them, particularly when they said that there would almost always be a record of extensive, progressive, pulmonary, lymph-gland, intestinal or other visceral tuberculosis. Very frequently, in infants and young children who had died of tuberculous meningitis coexisting with visceral miliary tuberculosis, the extent of the primary lesion was a small Ghon focus, with related glands that might even be difficult to find.

Dr. Webster said that this was the great difficulty that lay in the way of full acceptance of the view of Rich and McCordock by one like himself, whose work lay exclusively among infants and young children. MacGregor and Green had discussed possible ways in which the difficulty might be overcome, but time scarcely permitted of their consideration. One of the suggestions was that the meningitis might at times give rise to the miliary tuberculosis. Thus they found a very commonplace subject, on which finality appeared to have been reached long ago, again in the melting pot of speculation and research. The time at his disposal permitted him to do little more than draw attention to the situation.

Continuing, Dr. Webster said that he ventured to think that he was right in saying that to most of those present the term "disseminated tuberculosis" conveyed only one meaning, and conjured up a picture of miliary tuberculosis. Actually dissemination of bacilli was a frequent occurrence in tuberculous patients and miliary tuberculosis, but was its extreme clinical form. In patients with active focal tuberculous lesions, circulatory dispersion of tubercle bacilli took place very frequently. Clinical evidence of this was provided by the large number of cases of bone and joint and genito-urinary tuberculosis amongst persons who had never before shown any manifestations of the disease. It had to be allowed that in such cases the infection of first clinical importance came to the affected place by the blood stream, in a person who had had an unsuspected focus somewhere. It had to be considered, further, that when apparently primary kidney or bone tuberculosis did arise it was not likely that the bacilli that had induced those lesions had been the only detachment to traverse the bodily tissues by way of the blood stream. It was also probable that an actual spreading of bacilli by the blood in tuberculous infection in general was much more frequent than the number of cases that came to clinical appreciation would indicate. As Krause had stated, there was no more certain fact in tuberculosis than that the number of infections of any structure was many times the number of symptomatic foci, or that clinical disease of an organ developed once for every five, ten, or fifty times that bacilli lodged there.

There was now a natural approach to the second aspect of tuberculosis that Dr. Webster wished to discuss. If the view were correct that more or less frequent "seeding" of bacilli from an active tuberculous focus occurred, with concomitant low-grade, possibly intermittent and evanescent bacillæmia, then the kidney was exposed along with other organs, and was a favourable viscus in which to study subclinical and symptomless infection, because of the possibility of detection of tubercle bacilli in the urine.

Tuberculosis of the kidney, clinically manifest, and advanced to the stage of destruction and cavitation—renal phthisis—was very uncommon in children. He had been able to collect only half a dozen such specimens in the pathological museum in a period of twenty years. On the other hand, the frequency of tuberculous infection of the kidney, as distinguished from clinically evident tuberculosis, had been under-estimated in the past. There was no doubt that in association with other active hæmatogenous lesions, such as those of bones and joints, renal tuberculosis was not uncommon. In the early stages, which might persist for some years, there were no urinary symptoms whatever; pyuria was very slight and often intermittent, so that it would be overlooked unless careful and repeated examinations of the urine were made.

At the Hospital for Sick Children, Toronto, R. I. Harris had found tubercle bacilli in the urine of nine among 67 children affected with bone and joint tuberculosis. These children had no symptoms referable to the kidney or urinary tract. The only clinical sign that all was not right in the urinary system was a mild degree of pyuria, of microscopic dimensions. The existing state of affairs was disclosed by the routine injection of urine every two months into guinea-pigs. Prior to the institution of these measures tubercle bacilli had been detected in the urine of only one among 392 patients. The same observer, R. I. Harris, by means of routine guinea-pig inoculations, demonstrated the presence of tubercle bacilli in the urine of 37% of adult subjects of osseous tuberculosis.

Dr. Webster said that during the past eight months he had investigated specimens of urine from 26 subjects of bone and joint tuberculosis, patients of the Austin Hospital, and had been indebted to Dr. Hughes, resident pathologist at the Austin Hospital, for kindly collecting the specimens for him. He had recovered tubercle bacilli in culture from 11 of the 26—a proportion of positive findings of 42·3%—and in every instance the culture was obtained by direct cultivation, without the use of guinea-pigs. He was unable as yet to say how many of the eleven patients from whose urine a culture of tubercle bacilli was made, exhibited symptoms of renal involvement; but certainly some did not. The specimens had been collected with no regard to symptoms, it being sufficient that the patient was a subject of bony tuberculosis.

The frequent occurrence of symptomless tuberculous bacilluria could be taken as sufficiently proven; but was it possible that a state of excretory bacilluria could exist,

a condition in which tubercle bacilli were excreted by the kidney without any renal lesion's being induced? The answer to this question had to be in the negative. In the first place, it seemed improbable that the kidney could excrete tubercle bacilli with any greater facility than it could excrete any other form of particulate matter. Secondly, it was to be remembered that almost invariably, even though symptoms were absent, excess pus cells or a few erythrocytes were to be found in the urine, and the presence of these was indicative of a renal lesion.

The work of Helmholz, of Medlar, and more recently of David Band, furnished incontrovertible evidence against the theory of excretory bacilluria. Helmholz had shown that organisms were not found in the urine without renal lesions, and Medlar that after the intravenous injection of tubercle bacilli into animals, the bacilli were found in the urine only when demonstrable lesions were present in the kidneys, the lesions often being microscopical in size. Medlar also showed that of 30 patients dying of pulmonary tuberculosis, 22 had renal lesions, although none had displayed urinary symptoms before death. This particular research was planned on an heroic scale, and had involved the preparation and examination of 100,000 serial microscopic sections of the kidneys to be investigated. Again, the lesions were all small, often microscopical in size; in every case they were bilateral and—a very important observation—many showed indubitable evidence of healing.

More recently David Band, whose work appeared in *The Edinburgh Medical Journal*, in 1935, had investigated 174 cases of extraurinary tuberculosis for tuberculous bacilluria. In no case were there any symptoms; cystoscopic and pyelographic evidence of urinary tuberculosis was also lacking. From 25, or 14·4%, of the specimens examined, tubercle bacilli were isolated by animal inoculation. Again, it was to be noted that pus cells were present in excess in every specimen of urine from which a positive result was obtained. The kidneys of five patients in whom tuberculous bacilluria had been present were obtained at necropsy. No naked-eye evidence of tuberculous infection was found, but on microscopic examination of serial sections—no less than 1,500 to 2,000 from each half kidney—bilateral tuberculous lesions were found in each of the five cases.

Dr. Webster concluded by saying that he had digressed to some extent from the subject of renal tuberculosis in childhood, and it might be well if he returned to it by summarizing the principal points. Renal tuberculosis, appreciable clinically, was uncommon in childhood; but tuberculous infection of the kidney occurred frequently, especially in association with bone and joint tuberculosis. The infection was hæmatogenous, and at the outset was always bilateral. Cultural methods or guinea-pig inoculation afforded the only means of discovery in the many children who had no urinary symptoms and who might remain thus free for months or even years. Most important of all was the statement, well founded on the work of Medlar, that many of these early lesions healed. Dr. Webster showed a lantern slide prepared from a photograph of a culture of tubercle bacilli that he had grown from a specimen of cerebro-spinal fluid on the medium of Petragnani. Other lantern slides included a tuberculous kidney in a condition of renal phthisis, and a series of slides to show the macroscopic and microscopic appearances of a malignant hepatoma that exhibited teratoid features.

Medical Practice.

REPORT OF THE COMMITTEE APPOINTED TO OBSERVE THE KENNY METHOD OF TREATMENT FOR PARALYSIS AT LONDON.

WE have obtained the permission of the London County Council to publish the report submitted to the Medical Officer of Health of London by the honorary advisory committee invited to watch the treatment of patients with poliomyelitis and cerebral spastic paralysis demonstrated by Miss E. Kenny at Queen Mary's Hospital, Carshalton. The report, which bears the date of November 10, 1938, is as follows:

1. The period of one year having expired since Miss Kenny, with the Council's sanction, commenced the demonstration of her methods of care and treatment of poliomyelitis and of cerebral spastic paralysis, a report is now submitted on the subject.

The work commenced on July 13, 1937. A ward was evacuated and equipped as a clinic with the baths and other apparatus used by Miss Kenny and described by her in detail in her book entitled "Infantile Paralysis and Cerebral Diplegia", published by Angus and Robertson, Sydney, Australia, 1937.

Two adjoining wards (28 beds), and later a third ward (18 beds), accommodated the in-patients. There were also a small number of out-patients who have attended daily, every other day, or at such periods as were prescribed. The wards were staffed by members of the regular hospital nursing staff, whose numbers were somewhat increased beyond the hospital standard on account of the intensive care required day and night by Miss Kenny.

2. Miss Kenny brought with her two of her Australian trainees, who have assisted her continuously through the whole period, and there were appointed to complete the staffing five of the whole-time trained massage staff (with the part-time services of the massage superintendent) to learn the details of Miss Kenny's methods and work under her direction.

From November to April Miss Kenny herself had to return to Australia, and during this period delegated to Dr. F. H. Mills, M.B., B.S. (Sydney), who is familiar with the system, and to her senior trainee (Miss Grant) the supervision of the treatment. In this way continuity was preserved.

From the hospital side the whole unit was supervised by Mr. G. M. Gray, F.R.C.S., one of the Council's senior resident assistant medical officers, who has devoted his whole time to this work and to the careful observation of every one of the patients and to the detail of the treatment given.

3. In the first place the agreement with Miss Kenny was that her work should be demonstrated for three months, but at the end of that time it became obvious that this period was too short to form any reliable opinion as to the results of her treatment, and, accordingly, it was later agreed to extend the period to twelve months.

4. In view of the interest which has been aroused and the manifest importance of the whole matter, the Medical Officer of Health of the Council invited the assistance of orthopædic surgeons and neurologists to form an honorary advisory committee to watch the treatment carried on and to be associated with the Council's officers—Dr. H. O. West, M.D., F.R.C.P., D.P.H., Medical Superintendent of Queen Mary's Hospital, and Mr. G. M. Gray, M.A., M.B., Ch.B., F.R.C.S. (Edin.), F.R.C.S. (Eng.)—and the consulting orthopædic surgeon of the hospital (Mr. C. Lambrinudi, F.R.C.S.) in their conclusions.

There were accordingly appointed: Mr. H. A. T. Fairbank, D.S.O., O.B.E., M.S., F.R.C.S., Mr. R. C. Elmslie, O.B.E., M.S.., F.R.C.S., Mr. E. I. Lloyd, M.A., M.B., Ch.B., F.R.C.S., Dr. Macdonald Critchley, M.D., F.R.C.P.

5. In accordance with Miss Kenny's request for the admission to Queen Mary's Hospital of cases of poliomyelitis in the early stage of the disease, all such cases coming under the Council's care were admitted to this unit.

In addition, a number of cases selected by Miss Kenny of residual paralysis in poliomyelitis were transferred to her care and also a few cases of cerebral spastic paralysis which Miss Kenny considered were suitable for the demonstration.

In all, 63 patients have been treated as follows:

Poliomyelitis—	
(*a*) Recent (treatment commencing less than eight weeks from onset)	34
(*b*) Later (treatment commencing over eight weeks and less than twelve months from onset)	12
(*c*) Residual (treatment commencing over twelve months from onset)	9
	55
Cerebral spastic paralysis	8
	63

In general, Miss Kenny's treatment has not been interrupted or interfered with in any case except as the result of incidents (such as infectious diseases) which could not be controlled. Even in cases in which infectious diseases occurred, interference was avoided as far as possible by one of the trainees going daily to the fever hospital with the kind cooperation of the medical superintendent (Dr. J. S. Anderson, Grove Hospital).

6. Miss Kenny has claimed that she has obtained complete recovery in all recent cases of poliomyelitis which she has personally treated from the commencement.

> *Infantile Paralysis.*—All recent cases treated at the clinic (Townsville) have been totally and permanently cured. . . . It must be acknowledged that the number of recent cases of infantile paralysis at that time was very few, in fact, four only. During the last two years this number has been increased to twelve, with the same happy results. (*Ibidem*, page XXI, author's preface.)

Herein lies the importance of the admission of early cases already alluded to.

If we correctly understand from this that Miss Kenny claims to be able to cure poliomyelitis completely, then we are of the opinion as the result of our observations during the past year that such a claim is in no way substantiated.

7. There remain, therefore, the questions whether Miss Kenny's methods are better than customary methods, whether they yield better or more rapid results, and whether they should be recommended for general adoption.

These methods are enumerated as follows (*ibidem*, page 3):

1. Maintenance of a bright mental outlook.
2. Maintenance of impulse.
3. Hydrotherapy and remedial exercises.
4. Maintenance of circulation.
5. Avoidance of the generally accepted methods of immobilization.

These may now be considered *seriatim*.

(1) *Maintenance of a Bright Mental Outlook.*—We certainly agree that an optimistic outlook should be adopted both by the patient and those under whose care he is placed, but in a disease such as poliomyelitis this must be tempered by the judgement of clinical knowledge. Otherwise it is liable to become mere deception.

(2) *Maintenance of Impulse.*—We understand Miss Kenny to mean by this that the patient must be helped to make the mental effort to carry out a movement even when the muscles are so completely paralysed that no movement and no tightening of the muscles can be perceived.

We do not agree that any mental effort to produce muscular contraction can be felt by an attendant's hand, unless contraction actually occurs. Miss Kenny's "impulse" is presumably a minimal contraction of the muscle which may be so slight as to require experience in its detection. On the other hand, we agree that the voluntary contraction of muscles that have been paralysed or weakened should be encouraged by every possible means. This is, of course, in accordance with generally accepted views.

(3) *Hydrotherapy and Remedial Exercises.*—Miss Kenny's method of hydrotherapy is carried out in individual slipper baths or in a special "arm" bath. A warm bath is used with a hot and cold douche as a method of stimulation, and in it the limbs are exercised.

The principle of under-water exercises is not a new one, but in hospital practice is more often carried out in communal baths. The use of alternating hot and cold douches appeals to us as useful.

Miss Kenny sets out the merits of hydrotherapy:

(1) The circulation in the limbs and skeletal muscles is improved;

(2) their nutrition is maintained;

(3) the buoyancy of the saline water assists weak movements; and

(4) hydrotherapy improves the mental outlook (*ibidem*, page 7).

With this view we agree, and we think Miss Kenny's method is of value, but we cannot altogether accept her criticisms of the "communal bathing pool", which are as follows:

(1) The proximity of other patients causes distraction;

(2) the effort to keep afloat causes lessening of mental concentration;

(3) it is impossible to obtain the same degree of cooperation between the patient and attendant that the individual bath affords;

(4) a newly acquired movement may not be perceived as soon as it may be by the method of the individual baths, and through this oversight may be overtaxed and so weakened; and

(5) that hygiene is lacking (*ibidem*, page 7).

All these objections can be overcome. Large baths are no doubt to some extent unhygienic, but their use is limited to patients in hospital, and frequent changing of the water and simple hygienic measures are universally practised.

Actually we think there are certain objections to the small individual slipper baths. There is not room for certain movements, *e.g.*, abduction of the lower limbs, and the use of the principle of buoyancy is limited.

We must now refer to the important question of when remedial exercises (or muscle reeducation) are to commence. Miss Kenny strenuously advocates muscle reeducation as early as possible in the course of the disease and is not unwilling to practise this even before the cessation of pain.

Her method of reeducation consists essentially of passive movements which the child is invited to assist, if possible, by voluntary contraction of the appropriate muscles. It might be expected that such early movements would eliminate the incidence of stiffness so often seen when immobilization by splinting has been unduly prolonged. But we have seen stiffness arising quite early when no splint has been used. It does seem that real progress in passive mobility is only made when the pain has disappeared. Miss Kenny claims that her method of hydrotherapy, fomentations and passive movements helps to get rid of pain. Our observations upon this point are inconclusive, because the duration of pain in individual cases varies greatly.

(4) *Maintenance of Circulation.*—Miss Kenny attaches great importance to this, and we think rightly so. Though it is a matter which is usually attended to with care in individual cases at home, it has to be admitted that it should receive more attention in hospital practice. Among the ill-effects Miss Kenny ascribes to failure to maintain a good circulation are the following:

> (1) Loss of muscle tone.—This is well known to the massage profession, whose members find that they cannot get the muscles active until the limb has been warmed up.
>
> (2) Wasting.—This depends mostly on the extent of the damage to the nerve cells and the influence of peripheral circulatory factors is slight. In the cases

under review there certainly is wasting, but there is no doubt that the texture of the skin and subcutaneous tissues is good.

(3) Chilblains.—These also have not occurred, but we should say (i) that chilblains ought not to occur in such children who are in-patients in a hospital, and (ii) that they are late manifestations and are not usual in the first year.

(5) *Avoidance of the Generally Accepted Methods of Immobilization.*—In this principle Miss Kenny appears to differ fundamentally from what is described as the "orthodox" view. Dr. Mills, describing her method (*The British Medical Journal*, January 22, 1938, pages 168 to 170) summarizes "orthodox" methods of treatment:

> The accepted or orthodox methods of treatment may be summarized as follows:
>
> (*a*) Rest and immobilization of the affected limbs until the stage of pain or irritation is past.
> (*b*) Maintenance of affected muscles in a position of relaxation.
> (*c*) Avoidance of contractures and deformities by light retentive apparatus.
> (*d*) Massage and active and passive movements.
>
> Treatment along these lines is based upon the theory that the pain in the limbs is of central or meningeal origin. . . . In opposition to this accepted theory the view is taken that the pain in the extremities is almost completely vascular in origin.

While this summary may be generally accepted, it is necessary to point out that "orthodoxy" is not a precise term. Indeed, it is well known that orthopædic surgeons differ widely in the practical application of the principles of splinting and immobilization; so that when "immobilization" is spoken of and condemned by Miss Kenny as if it were the habit of all orthopædic surgeons to place children on a retentive frame or in splints without any other treatment for an indefinite period of time, even extending to months, and the production of deformities is ascribed to the splints themselves, her view is inaccurate.

While we should agree that "immobilization" may be practised overlong, we are opposed to Miss Kenny's refusal to use any splint at all in the treatment of this disease. All retentive splintage must be used intelligently and with discretion as a means to an end and not merely as an end in itself. Miss Kenny claims that the initial period of rest and immobilization is unnecessary, and adheres to the "theory of natural posture in correct alignment without immobilization", meaning thereby that the body and limbs should be kept in their natural position in the intervals between exercises. This she aims at maintaining by the constant attention of the trainees or nurses, and by means of pads and slings and boards at the end of the bed to prevent "footdrop". She thus uses "position", but will not adopt the use of splints to maintain it.

Apart from some degree of contracture of the *tendo Achillis* in a few cases which was overcome later, we have seen the development of no contractures while the patients were recumbent and well supervised, nor have we found evidence that her refusal to put the paralysed muscles in the position of relaxation has caused delay in the initial return of power.

We think, therefore, that it must be admitted that Miss Kenny's method of keeping limbs in a neutral position without splints when in bed is not harmful in the early stages of the disease, and, in fact, has this to commend it: that it spares the children the irksomeness of splints at that stage.

On the other hand, we are as definitely of the opinion that when a muscle is recovering, splints are often useful in preventing over-fatigue and deformity. It follows from this that we think Miss Kenny's prejudice against splints and appliances leads her to keep the children recumbent unnecessarily long, when the judicious use of an appliance might enable them to get about earlier with no harm to the muscles and joints, and even with benefit to the muscles and to the child generally.

It is certainly vital to Miss Kenny's system that there should be constant supervision. Such intensive care seems only possible in an institution specially equipped and staffed for the purpose.

8. With these five "principles" in view, Miss Kenny uses "exercises and other procedures for the restoration of functional power to apparently paralysed muscles". It is not, we think, necessary to describe in detail her methods of "muscle reeducation". They are simple, and can be carried out by trainees who have not been as fully instructed in anatomy and physiology as are members of the massage profession. We have seen nothing to suggest that Miss Kenny has designed methods superior to those used by the massage profession. In fact, we consider it is legitimate criticism of her method that it does not include a number of useful measures practised, certainly in this country, by experienced masseuses.

As we have already observed, Miss Kenny's system involves that such muscle reeducation should be commenced in the early stages, and should be continued throughout the treatment, and she claims on its behalf that it maintains the dormant normal impulses which she believes wither under immobilization methods and may die beyond the hope of resuscitation. Careful graduation of exercise as practised by her avoids over-fatigue and in this she follows well-established practice.

Treatment by early movements, it must be noticed, is being practised in several other centres abroad. We have seen no evidence that the early movements in the cases we have observed have been harmful, but neither have we reason to think that they have specific value in determining the degree of restoration of useful function. This method has perhaps encouraging psychological effects which may be beneficial. It is noticeable that in some of the severe cases treated from an early stage all the efforts of Miss Kenny and her staff have failed to bring back any movement in the paralysed muscles.

9. Twelve months is too short a period in which to assess finally the question of residual paralysis. In our view, Miss Kenny has not really faced this issue. If we understand her aright, she believes that under her system in two—or perhaps three—years' time her patients will not require artificial aids, and, having sufficient useful function, will not require any surgical supervision or after-care.

We wish we could believe this to be true. It is, of course, well known that some patients with poliomyelitis recover to a considerable degree under any system of treatment, and that they may continue slowly to improve for a long time; but so far as our twelve months' observation of this very interesting experimental period has gone, we have seen nothing whatever to justify Miss Kenny's belief. We have been specially interested in her opinion, expressed late in the year, that she is satisfied if she can get partial recoveries, *e.g.*, in an arm case she aims at a "good forearm" and in a leg case at "good gluteal muscles", leaving stabilizing operations to the surgeon. This differs little from the accepted view in this country. In this she seems to abandon her claim to effect a complete cure.

10. It is necessary, we think, to refer only briefly to Miss Kenny's treatment of cases of cerebral spastic paralysis. By her extreme attention to detail, incessant and intensive application, coupled with most admirable patience and optimistic enthusiasm, Miss Kenny has achieved some amelioration in the cases under treatment. But there is nothing original in the principles of her treatment, and it is very doubtful whether any of the more severely affected patients treated can ever become self-supporting. In our experience of these cases, improvement of some sort under any intensive system of training or treatment frequently occurs. No doubt, this is encouraging to the relatives of these patients, but relapses are not infrequent following the cessation of treatment.

11. We may conclude this report by some general observations. We have indicated our view that this system is not the last word in the treatment of poliomyelitis. (We disagree with Dr. Mills's enthusiastic support, and feel bound to record our opinion that it was unfortunate that his article on the subject—*The British Medical Journal*, January 22, 1938, page 168 *et sequens*—was published during the course of this investigation.) At the same time, no one can be complacent about this distressing disease, and we should be ready to adopt any method of

proved value and incorporate it in "orthodox" treatment, so-called. Miss Kenny herself has consistently expressed her desire to be of service through regular medical channels.

We should therefore have no difficulty in recommending —certainly for an extended period—the continuation of Miss Kenny's system of hydrotherapy in the poliomyelitis unit of this hospital. Having expressed the opinion that this is of value, it would seem foolish not to use the apparatus which has been installed. We see no difficulty and no inconsistency in incorporating this part of Miss Kenny's system, for instance, in a major scheme of treatment which would include splintage where this is thought advisable.

We are in no doubt as to the value of the segregation of cases of poliomyelitis in large special units. This was originally suggested to the Council by Mr. Elmslie, and resulted in a unit at Queen Mary's Hospital, with a preliminary period at the Western Fever Hospital because of the supposed risk of infection. The present series of cases seems to have shown that no disadvantage has followed the transference of cases to Carshalton at an earlier stage than hitherto, and we should be glad to see the intensive treatment, which has resulted from Miss Kenny's visit, continued. Though it is incapable of proof, we believe there is no appreciable risk of infection—an opinion which agrees with the generally accepted views on the subject.

Certainly we hope that arrangements will be made for the continued observation of these particular cases for reasons already indicated.

12. We should therefore sum up our main conclusions as follows:

1. We have seen no reason to admit Miss Kenny's claim that complete cure can be promised in any group of cases of poliomyelitis.

2. We consider that the use of hydrotherapy in the form of hot and cold douches as practised by Miss Kenny is of value.

3. We consider very early attempts to initiate voluntary movements and also early and frequent passive movements are harmless, but of unproven value. We think, however, it is a legitimate criticism of her method generally that it does not include a number of useful measures practised, certainly in this country, by experienced members of the massage profession.

4. We agree with Miss Kenny that under certain conditions, which we have specified, splints can be dispensed with in the treatment of the early stages of the disease. We do not approve, however, of her entire abolition of splints and surgical appliances in treatment. We consider that they are often valuable and sometimes essential parts of treatment; but, on the other hand, we are equally sure that the mechanical methods which she employs in substitution for splints are inadequate. We would add, however, that we disagree with the long periods of continuous mechanical immobilization which are sometimes imposed.

5. We consider that Miss Kenny has not really faced the issue of residual paralysis for which we believe surgical appliances or surgical methods, such as stabilising operations, offer the only eventual hope of amelioration.

6. Some improvement appears to have been achieved in the cases of cerebral spastic paralysis treated, but Miss Kenny's system demonstrates no original principles.

(Sgd.) H. A. T. FAIRBANK.
(Sgd.) MACDONALD CRITCHLEY.
(Sgd.) E. I. LLOYD.
(Sgd.) C. LAMBRINUDI.
(Sgd.) M. C. ELMSLIE.
(Sgd.) GEO. M. GRAY.
(Sgd.) HENRY O. WEST.

Miss Kenny's Comments.

Extracts from Miss Kenny's comments on this report are as follows:

The summing up of the Royal Commission of Investigation of the treatment of infantile paralysis is in strict accordance with the recognized orthodox treatment and collected evidence from other countries. The primary treatment is splinting and rest. This statement is also announced in *The British Medical Journal* of December 17, 1932. The method introduced to Queen Mary's Hospital was the exact opposite and embraced the treatment of all symptoms immediately they became evident, principally pain and muscle spasm. It was noted when splints were abandoned and this method of treatment given in the early stages, that pain, muscle spasm and contractions causing deformities soon disappeared. It was unfortunate that the Royal Commission in Queensland did not have the same opportunity of observing the work as did the committee of investigation.

The committee states that there has been no delay in the initial return of power. This committee was in a very satisfactory position to make this announcement as cases treated by the orthodox methods were on the premises, and muscle tone circulation and joint condition with initial return of power were not nearly so satisfactory. The latter was omitted, but the film picture shows this statement to be correct.

The committee of investigation, London, admitted that with the Kenny method of treatment no contractures had occurred, with the exception of slight contractures of *tendo Achillis*, which were quickly rectified. These contractures occurred during my absence in Australia through muscle spasm not being attended. When the spasm was treated in the heads of the gastrocnemius muscle the tendon relaxed. To sum up, it must be admitted that the accepted orthodox method, with its attendant system of reeducation, did not give as satisfactory results as the Kenny method.

The committee agrees with all the principles laid down in the book which was written for the direction of treatment of residual paralysis. It is interesting to know that during the last two years 220 recent cases of infantile paralysis have been treated by this method, and there has not been a deformity or contraction in the whole number, and all deformities were corrected by this method if transferred from the orthodox within six months of the onset.

The committee admits that the skin and subcutaneous tissue of the patients were in a very good condition, and also allude to the fact that in the orthodox method the paralysed part is usually warmed by the masseuse before treatment. This is usually done by the application of heat or massage. In reply to this, I wish to state that heat alone will certainly bring the blood to the surface, but will not induce circulation. As a matter of fact, I have noticed at Queen Mary's Hospital in the patients receiving orthodox treatment where this method of warming the part had been practised, the limbs resume their blue and cold appearance immediately the patients return to their beds, while the patients receiving Kenny treatment are warm and comfortable owing to the fact that the circulation has been induced by the correct method of expansion and relaxation of muscle fibre.

I think that with all these admissions it must be admitted that orthodox treatment has not produced the results hoped for, and if a further research could be made by men of science to investigate the signs and symptoms brought before the notice of the medical profession by my work, and previously left unnoticed and unattended, something much greater could be done.

I did not demonstrate the treatment of spastic paralysis to the committee, as I was not requested to do so; but I demonstrated the method to several other visiting medical men, who agreed that the method was just the opposite to that practised by the medical profession both in England and America. The film picture shows improvement in cases that had up to ten years' consecutive treatment with no improvement in English hospitals.

It is rather to be regretted that this committee was not appointed from the time of the opening of the clinic, as quite a lot of contractions and deformities had been corrected by this method which had developed during orthodox treatment in an adjacent ward. This also can be seen in the film picture, and quite contradicts the statement made by the commission that useful exercises

were used by orthodoxy in these cases which were omitted in my method. If the exercises had been useful, these contractions, which have admittedly occurred according to the report of this committee and the Royal Commission during orthodox treatment, would not have been in evidence.

These corrections of contraction and deformity occurred in patients suffering from both infantile and spastic paralysis.

The patients under review had had upwards of five months' treatment before the committee was formed. This treatment (which is the treatment of early cases of infantile paralysis) was not demonstrated to the committee. All of their ideas of treatment were absorbed from the book, which is, as already stated, the treatment for residual paralysis. It must be admitted that the treatment which will allow initial return of power, prevent contractions and deformities, and rid the patient of pain and stiffness, must be the more satisfactory.

It is regrettable that no allusions have been made to certain signs and symptoms in this disease which require investigation by research, and until this is done, in my opinion, no treatment will be as satisfactory as it should be.

The Royal Australasian College of Physicians.

INAUGURAL CEREMONY.

The Inaugural Ceremony of the Royal Australasian College of Physicians took place in the Great Hall of the University of Sydney on Wednesday, December 14, 1938. In the presence of an audience numbering about one thousand the ceremony was carried out with impressive ritual, which was all the more important and interesting because it established a precedent for the formal procedure of the college.

A programme of carillon music was played from 7.40 p.m. till 8.15 p.m. on the Memorial Carillon by Mr. J. D. Gordon, B.A., L.R.S.M., the Honorary Carillonist of the University of Sydney. This was followed by a programme of organ music in the Great Hall from 8.15 p.m. till 8.30 p.m., played by Mr. G. Faunce Allman. At 8.15 p.m. His Excellency the Governor of New South Wales, Lord Wakehurst, and Lady Wakehurst arrived and were met by the President, Sir Charles Blackburn, with Dr. S. V. Sewell and Professor D. W. Carmalt-Jones (Vice-Presidents). Lady Wakehurst, who was accompanied by Miss Morna McKenzie, was escorted to the hall by Professor Carmalt-Jones, while His Excellency, who was attended by Captain K. O'B. Harding and Captain R. E. Loder, proceeded to the Senate Room. Here a procession was formed. Mr. W. A. Selle, M.A., Registrar of the University of Sydney, acted as Esquire Bedell, and the councillors of the college, the representatives of other colleges, the Chancellor of the University of Sydney, Mr. Justice Halse Rogers, the Deputy Chancellor, Dr. A. E. Mills, and the President preceded His Excellency the Governor, and, entering the hall by the eastern door, took up positions on the dais.

Among those seated on the dais were the Lieutenant-Governor, Sir Frederick Jordan; the Right Honourable Sir Earle Page, G.C.M.G., M.P., Minister of State for Commerce, representing the Federal Government; the Honourable H. P. FitzSimons, Minister for Health, representing the Government of New South Wales; the Honourable Sir George Rich; His Excellency the Most Reverend John Panico, S.T.D., Apostolic Delegate to Australasia; the Most Reverend N. T. Gilroy, D.D., Coadjutor Archbishop of Sydney; the Venerable Archdeacon Begbie; the Right Reverend E. Norman McKie, B.A., Moderator of the Presbyterian Assembly of New South Wales; the Reverend R. H. Campbell, President of the Methodist Conference of New South Wales; Commissioner W. Dalziel, of the Salvation Army; Justices of the Supreme Court of New South Wales; Judges of the District Court of New South Wales; the members of the Consular Corps and their wives, headed by the Dean of the Consular Corps, Dr. G. L. Host and Mrs. Host; the Lord Mayor, Alderman N. L. Nock; representatives of the Military and Naval and Air Forces; other Government representatives; representatives of the British Medical Association, including Sir Henry Newland, President of the Federal Council of the British Medical Association, and Dr. B. T. Edye, President of the New South Wales Branch of the British Medical Association; office-bearers of the Royal Australasian College of Surgeons; Senators of the University of Sydney and members of the professorial staff of the University of Sydney. The large audience in the body of the hall included many distinguished guests, among whom were the wives of the officials and councillors of the college, wives of the other official guests, benefactors of the college and their wives, civic representatives, representatives of the Hospitals Commission of New South Wales, of other professional associations, of Government departments, and of the Press, and the Fellows of the Royal Australasian College of Surgeons and their wives.

President's Address.

The President, Sir Charles Bickerton Blackburn, delivered the following address.

Your Excellency, the honour has devolved upon me, as President of the Royal Australasian College of Physicians, as the temporary representative of the two great Dominions of Australia and New Zealand, to offer you a most cordial welcome, both personally and on behalf of the many Fellows and members who constitute the Royal Australasian College of Physicians.

We desire to convey to His Majesty the King through you, his representative, our loyal devotion to his service and our firm resolve that this college shall at all times and in all respects prove worthy of the Royal title that His Majesty has graciously bestowed upon it.

It is my pleasing duty to extend a welcome to Lady Wakehurst; the Lieutenant-Governor; the Chancellor of the University of Sydney; the Deputy Chancellor; the right Honourable Sir Earle Page, Minister of State for Commerce; the Honourable Herbert FitzSimons, Minister for Health of New South Wales; the Lord Mayor, Alderman Nock; and the many others who have honoured us by accepting our invitation to attend this ceremony.

Momentarily included in the term "others" are some whose names I have been, as it were, keeping behind my back in order that I may hold them up the more conspicuously for a special type of recognition, and, first, I shall again mention the Chancellor, Deputy Chancellor and members of the Senate of the University of Sydney, who are our hosts tonight. To welcome the Chancellor, His Honour Judge Halse Rogers, to this famous Great Hall of his own university would be so like welcoming a king to his castle that I will compromise and say that it is very gratifying to see him at this ceremony, and this is not merely because it affords me an opportunity of thanking the university through him for being allowed to meet in this historic setting, but because his presence symbolizes the harmonious cooperation between the Australasian universities and this college, linking up undergraduate and post-graduate education. There is no ambiguity about the use of the word "welcome" when speaking of the Royal College of Physicians of London, that famous institution that has, ever since its foundation in 1518 by King Henry VIII, been regarded as the backbone of British medicine and has served as the pattern and god-parent of all similar institutions founded among English-speaking people. We gratefully acknowledge the sympathy, encouragement and advice we have received from the college in framing our constitution, and regard the presence with us tonight of so distinguished an executive officer of the college as a supreme gesture of goodwill. I am indeed proud to be able to announce that this famous English physician has consented to be elected as the first honorary Fellow of the college.

Professor Lambie, one of our own members, needs no introduction from me; but I do not want to think of him in his normal capacity, but as a Fellow of the Royal College of Physicians of Edinburgh; for he is here as the representative of that ancient college. I hope I shall not be regarded as unduly egotistical when I say that I believe that in selecting Professor Lambie as its delegate the Royal College of Physicians of Edinburgh has honoured not only the Bosch Professor of Medicine, but also the University of Sydney.

Another visitor from overseas whom we very warmly welcome is Dr. Noble Wiley Jones, of Oregon, in the United States of America, who brings greetings from the American College of Physicians, of which he has the honour to be second Vice-President. We are deeply sensible of the high compliment the American college has paid us in sending as its ambassador one who not only holds this high executive position, but who, as a physician, has achieved world-wide repute for his researches into vascular disease. That Dr. Jones has honoured us by consenting to be elected to honorary fellowship has resulted in a very pleasing and, I hope, significant relationship between Great Britain and the United States of America in the pages of our register.

From nearer home, I now hold up a very well-known name, that of Sir Hugh Devine, who is representing our elder brother, the Royal Australasian College of Surgeons, of which he is senior Vice-President, and in welcoming him, it gives me great pleasure to have this opportunity of saying how greatly the Council is indebted to him and his colleagues for advice and help in framing our constitution.

No one presiding at any medical function can fail to be gratified to see present the leaders of the British Medical Association, a body to which the public of these two dominions are so completely indebted for an efficient and well-organized medical service that they tend to accept it as a part of their lives and criticize it as freely as any other part of their environment. We are honoured tonight by the presence of two very distinguished representatives of the Association, Sir Henry Newland, President of the Federal Council, and Mr. Benjamin Edye, President of the New South Wales Branch.

One other whom it gives me very great personal pleasure to welcome is my commanding officer, Major-General Rupert Downes, Director-General of the Medical Services of the Commonwealth. General Downes has paid us a very great compliment in being present tonight, and I should like to assure him that he can, on all occasions, rely upon receiving the loyal support of this college.

Your Excellency, you have been invited here tonight to set the seal to a great endeavour. The formation of the Australasian College of Physicians is no hastily conceived project, but the final stage in a carefully thought-out plan. That plan has emanated from a little-known but very notable body, the Association of Physicians of Australasia. Unheralded and hitherto unsung, this association has played a brief but very important part in the development of medicine in these two dominions. It was founded in 1930 as virtually a private club, and its restricted membership was eagerly sought by the leading physicians of Australasia, and it was through the contacts and understandings that resulted that there developed that unity of purpose that made the constitution of so far-flung a college possible.

In the actual development of the college, the greatest encouragement has been received from the Commonwealth Government of Australia and the Government of the Dominion of New Zealand, while most generous financial assistance has been given by the Government of New South Wales and many private benefactors, whose names will be found on the programme. I shall refer also particularly to Sir Alfred Davidson, Sir John McKelvey, Mr. Martin McIlrath and Mr. Frank Packer, who gave much time and most valuable advice to the committee engaged in organising a public appeal.

To inform Your Excellency of the objects of the college as set out in appropriate legal form under twenty-three headings would be an unfair test of endurance. Briefly epitomized, the essential purpose is the promotion by all means in its power of the scientific approach to the study of disease. In achieving this purpose, it proposes to concern itself especially in fostering and cooperating in all undertakings designed to provide facilities for young graduates to acquire advanced knowledge in medicine.

It is also proposed to continue the activities of the Association of Physicians in arranging regular meetings of Fellows and members, where personal contacts will be made and scientific discussions held. On these occasions it will, from time to time, arrange for the delivery of public lectures on medical subjects of general interest, a practice which is to be initiated this evening by the distinguished delegate from the Royal College of Physicians of London, Dr. Herbert Morley Fletcher.

I firmly believe that this distinguished gathering you are about to address is wishing god-speed to an organization destined to exercise a vast, quite incalculable, but ever-increasing influence in improving the health and lengthening the years of the people in these two great dominions. It is therefore with the utmost confidence that history will account this the most notable undertaking embarked upon during the sesqui-centenary year of the foundation of New South Wales that I now have the honour to invite Your Excellency to inaugurate the Royal Australasian College of Physicians.

Address by His Excellency the Governor of New South Wales.

His Excellency the Governor of New South Wales, Lord Wakehurst, then spoke as follows:

Sir Charles Blackburn, Fellows and Members of the Royal Australasian College of Physicians, Ladies and Gentlemen: A message has been received through the Governor-General from His Majesty the King. I would ask you to stand while I read it:

> I greatly appreciate the loyal assurances which you, on behalf of the Council, Fellows and members of the Royal Australasian College of Physicians, have addressed to me on the occasion of the Inaugural Meeting at Sydney. I wish the college all success, in confident belief that it has a great future before it and that its establishment will contribute materially to the advancement of medical science in Australia and New Zealand.—George, R.I.

I am also asked to deliver messages from the Governor-General of Australia and the Governor-General of New Zealand, in the following terms:

> I regret my inability to be present at the inaugural ceremony of the Royal Australasian College of Physicians and to welcome the delegates present. I feel sure that the discussions and the pooling of knowledge which will take place will lead to advance in diagnosis and treatment of the sick and that your reward will be the gratitude of mankind. I wish your conference every success.—Gowrie.

> I desire to convey to the President, Fellows and members of the Royal Australasian College of Physicians present at the inauguration of the college at Sydney on December 14 an expression of my continued interest in the most important work in which they are engaged, and my very best wishes for a successful meeting.—Galway.

Ladies and Gentlemen: The close relationship which existed between the Universities of Oxford and Cambridge and the Royal College of Physicians of London at the time of its foundation, 420 years ago, in 1518, makes it especially appropriate that the inaugural ceremony of the Royal Australasian College of Physicians should be held in the Great Hall of the University of Sydney. Tonight, once again, but on the opposite side of the earth, an elder institution assists at the birth of a new member of the academic family. Thus emphasis is laid on the unity of purpose between two educational bodies, which, though different in type and scope, are one in ideals.

The constitution of the college whose inauguration we are celebrating is closely modelled on that of its prototype, the Royal College of Physicians of London. That body has exercised a profound and ever-increasing influence on British medicine. We are confident that our Australasian college will be able to live up to the example and standards which it has chosen to emulate.

The Royal Australasian College of Physicians is unique in that its territory extending over three and a quarter million square miles is greater than that of any other college of physicians in the British Empire. I feel sure that the Council will realize the magnitude of its responsibility and the great trust committed to its hands. I take this opportunity of congratulating Sir Charles Blackburn on being the first President of this college; and just as we recall Thomas Linacre as the first of a long line of illustrious presidents of the Royal College of Physicians of London, so we can imagine future generations of Fellows regarding with pride a long succession of honourable names headed by the present wearer of the presidential gown.

Incidentally, I am told that the name of Blackburn twice appears in the early records of Fellows of the Royal College of Physicians of London. I do not know whether Sir Charles claims any relationship; but it would be pleasing if this personal link could be established with the first occupant of the Australasian presidential chair.

We all know how much the Royal Australasian College of Surgeons has already done to raise the standard of surgical practice throughout Australia and New Zealand. It will be for the Royal Australasian College of Physicians to perform a like service for its branch of the medical profession. In this connexion, may I put in a plea for the encouragement of research as well as for the diffusion of existing knowledge? Research is the life-blood of medicine as of all science. A body such as yours, as I have said on another occasion about this university, will only be completely achieving its purpose if it is continually pressing against the furthest bounds of knowledge and striving to extend them.

One very important result of the formation of this college will be to bring physicians from widely separated places into personal relationships. I am glad that the college has recognized that its responsibilities do not end in awarding recognition to professional excellence, but that the constitution has provided that there shall be frequent opportunities for discussion and mutual help. Such meetings will not only tend to lessen the feeling of physical isolation which is inseparable from so far-flung a constituency. They will do much more: they will encourage the impact of mind upon mind so as to remove the still greater disability of intellectual isolation; they will contribute to the spread of recent advances in medicine, and they will unite the exponents of the physician's art in the bonds of understanding and friendship.

Finally, it is the desire and hope of all of us that this college, inaugurated tonight amidst these noble surroundings, shall grow from strength to strength, shall gather unto itself wealth of inspiring tradition, and become another powerful weapon in the never-ending fight against the bodily ills that beset mankind.

Address by the Right Honourable Sir Earle Page.

The Censor-in-Chief, Dr. S. O. Cowen, then asked permission of the President to call upon the Right Honourable Sir Earle Page, Minister of State for Commerce, to deliver his address.

Sir Earle Page said that the Prime Minister regretted his inability to be present personally on the occasion of the inauguration of the college. Sir Earle Page thought that he had been asked to represent the Federal Government because of his own personal association with the medical profession, and he was very glad to be present to be able to congratulate the college on its successful inauguration. He said that the Royal Australasian College of Physicians was fortunate in having obtained the honour of the title "Royal" at the beginning of its career, the physicians in this respect being more fortunate than the surgeons. He felt sure that the new college would exert a definite influence for good in Australia and New Zealand and help the medical profession to bring their knowledge to bear with greater effect upon the problems of health. Chief among these problems was that of the prevention of disease, and he hoped that the study of the practice of preventive medicine would be in the forefront of the activities of the college that began its career that night.

Address by the Honourable H. P. FitzSimons.

The Censor-in-Chief then called upon the Honourable Herbert P. FitzSimons, Minister for Health of the State of New South Wales, to deliver his address. Mr. FitzSimons expressed his pleasure that the Government of New South Wales had been able to help the college to establish its headquarters at Sydney. He pointed out that two recent outstanding events of great importance, not only to the medical community but also to the whole of the people of the State, were the establishment of a post-graduate school at the Prince Henry Hospital and the foundation of the Royal Australasian College of Physicians. He looked forward confidently to the great influence which would undoubtedly be felt in the health and well-being of the community, and felt sure that the physicians would carry out their responsible duties with a broad outlook of service to the public and that this service would in a few years reach a standard that had hitherto not been attempted in this country.

Introduction of Members.

The Censor-in-Chief then introduced the recently admitted members, as follows:

Your Excellency, Mr. President: I now present to you those members of the college who, after examination by a Board of Censors, were admitted to membership at a meeting of the Council held on December 13, 1938. They are the first members of the college; their names stand at the head of the Roll of Members, a roll which, we believe and trust, will lengthen indefinitely in years to come.

The members present were as follows: Dr. J. F. Akeroyd, Dr. P. M. Anderson, Dr. C. G. Bayliss, Dr. S. G. Bradfield, Dr. T. C. Butler, Dr. R. R. Bye, Dr. I. T. Cameron, Dr. N. C. Cunningham, Dr. M. C. Davis, Dr. N. L. Dodd, Dr. L. Holland, Dr. J. B. McMiken, Dr. I. S. Magarey, Dr. J. T. Paton, Dr. H. M. Rennie, Dr. C. W. Ross, Dr. B. A. Serjeant, Dr. B. T. Shallard, Dr. R. Southby, Dr. S. E. L. Stening, Dr. D. G. R. Vickery, Dr. C. Yeatman.

They advanced to the dais, and were presented in turn to His Excellency the Governor and the President.

Messages from Other Colleges.

The Censor-in-Chief asked the representatives of other colleges to deliver their messages of greeting to the college.

The Royal College of Physicians of London.

Dr. H. Morley Fletcher delivered the message from the Royal College of Physicians of London, as follows.

Your Excellency and Mr. President: I feel it is a very great honour to come before you today as the representative of the Royal College of Physicians of London to act on behalf of its President and Fellows. Dr. Robert Hutchison, owing to his recent appointment as President and to the onerous duties he has undertaken in that capacity, is unable to be present as he would have wished. He has asked me to give you the following special message of greeting and good wishes:

> It is a great disappointment to me that I am unable to be present in person on this historic occasion, especially as I have such pleasant recollections of my visit to Australia three years ago and of the great kindness and hospitality which I enjoyed at that time.
>
> It is my earnest hope that the Royal Australasian College of Physicians may long continue to flourish, and I desire—in the words which I have to address to each new Fellow of our own college—to wish its President, officers and Fellows "all happiness".—R. Hutchison, P.R.C.P.

And now I have a further duty to perform. One of the most cherished possessions of the Royal College of Physicians is the silver wand or caduceus which was presented to the college by Dr. John Caius, President in 1555. This emblem of authority is carried by the President on official occasions, and during the meetings of the college is placed on a cushion in front of his chair. I may say for the benefit of those who are unaware of the fact, the name, though spelt Caius, is pronounced "Keys". Caius was President for eight years and is perhaps best known as the founder of Gonville and Caius College, Cambridge, a college always closely associated with the study of medicine. The figure of Dr. Caius may be seen in the top left-hand corner of the window at the east end of this hall. The word caduceus means a herald's wand and was the staff or wand borne by Hermes or Mercury, the messenger of the gods. This, which is an exact replica of the original one, I now present to you, sir, on behalf of the Royal College of Physicians of London, as a token of close fellowship between the two colleges. May it be borne by successive presidents for many years to come.

I also present on behalf of my college the three volumes of Munk's Roll, which is a list of the Fellows from its foundation in 1518 to the year 1825, and a facsimile copy of Harvey's notes.

Finally, I have been entrusted with this address to the Royal Australasian College of Physicians, which I will now read:

> We, the President and Fellows of the Royal College of Physicians of London, desire to send to the Royal Australasian College of Physicians our fraternal greetings and our hearty congratulations upon its successful inauguration. We have watched with much sympathy the steps that have been taken to bring the new college into being and have regarded it as a privilege to put the long experience of our college at the disposal of its founders. We do not doubt that the establishment of the Royal Australasian College of Physicians in Australasia will not only promote learning and good fellowship among physicians in that part of the Empire, but will also be in the highest interests of medical science and practice.
>
> Along with this address, we have great pleasure in presenting the new college with a replica of our ancient caduceus, one of the insignia of office of our President. In the words of the original designer, Dr. Caius, the silver rod indicates that the President should rule with gentleness and clemency, unlike those of old time, who ruled with a rod of iron. The serpents, the symbols of prudence, teach the necessity of ruling prudently, while the arms of the college placed on the summit indicate that gentleness and prudence are the means by which the college is sustained.
>
> We are confident that the Royal Australasian College of Physicians will always be guided by these principles and we cordially wish for it a long and useful and prosperous existence.

The President replied as follows:

Dr. Fletcher: As President I desire you to convey to the President and Fellows of your great college the thanks of the Fellows and members of this college for these additional tokens of their sympathy and regard. This letter from your distinguished President, this address, and these precious volumes will be for all time treasured in our archives, while this chaste replica of your caduceus will remind our presidents not only of our filial relationship with the parent college, but of their obligation to discharge their duties with honour and dignity comparable with that of those who have carried the original.

The Royal College of Physicians of Edinburgh.

Professor C. G. Lambie, as representative of the Royal College of Physicians of Edinburgh, delivered the message from that college, as follows.

Your Excellency, Mr. President, Fellows and Members of the Royal Australasian College of Physicians, Ladies and Gentlemen: On behalf of the Royal College of Physicians of Edinburgh, I wish to convey to you the good wishes and congratulations of my college and to welcome the Royal Australasian College of Physicians as a sister college. My President desires me to say that he regrets his inability to be present to offer you his blessing. For my part, I must confess that I am conscious of a certain degree of embarrassment in the discharge of my commission, because, as a foundation Fellow of the new college and at the same time the representative of a very ancient college, I rather feel like one who is called upon to act as godfather to his own offspring.

Thus doubly honoured, I can but express the hope that this newly born child may grow up in the faith and traditions that have guided its predecessors; that it may have a long and distinguished career of usefulness to the community and that it may serve to inspire and to illumine the profession of medicine.

I have now great pleasure in announcing that, as a token of goodwill and respect, the Council and Fellows of my college have decided to confer upon your President, Sir Charles Bickerton Blackburn, the Honorary Fellowship of the Royal College of Physicians of Edinburgh.

The President replied as follows:

Professor Charles Lambie: As President of this college I desire you to convey to the President and Fellows of the Royal College of Physicians of Edinburgh the grateful thanks of this college for its messages of goodwill. I also desire you to convey our thanks for the great honour conferred on this college by the conferring of the honorary fellowship of your college on the first President of this college of ours.

On this exceptional occasion I will, with Your Excellency's permission, figuratively disrobe, and, in the garb of a simple physician, express through Professor Lambie my profound gratitude to the Royal College of Physicians of Edinburgh for the great distinction they have conferred upon me.

The American College of Physicians.

Dr. Noble Wiley Jones, as representative of the American College of Physicians, delivered the message from that college, as follows.

Your Excellency, Mr. President, Mr. Chancellor, My Lord Mayor, Fellows and Members of the Royal Australasian College of Physicians, Ladies and Gentlemen: On behalf of the American College of Physicians, I have the honour to extend to the Royal Australasian College of Physicians, its officers, Fellows and members our greetings and our congratulations and our good wishes for the success of your inaugural meeting and your future.

We know full well that your college can and will advance in many ways the cause of scientific medicine throughout Australasia. Just as our American College of Physicians has brought the medical men of Canada, the United States and the smaller American countries into a closer bond of fellowship and mutual understanding, so is it possible and important that you help to do the same in your own countries. It is important that the medical men of all English-speaking nations do likewise, to the end that we may be more closely united in the common effort of ensuring peace and maintaining our civilization in this troubled world. The great burden falls now upon the British nations, but I can assure you there is a growing awakening among the people of the United States of America, a growing feeling that all English-speaking peoples must stand together, that before long our people will discard their provincialism and stand shoulder to shoulder with the people of the British Empire in order to carry through this necessary task.

In recent years, we, in America, have been following the clinical and research work of your physicians more closely. Each year a few of your members have honoured us by their visits, and we have learned to know them as well as their work. It is one of the aims of the American college to foster these contacts and to make your visits more pleasant and profitable. We shall try to reciprocate also by urging more of our members to visit your medical centres and to meet you personally. We hope that your

visits to us will increase in number year by year and will give you as much pleasure as we shall enjoy your coming. Remember that the services of the executive officers of the college are open to you at all times and every member of the college, wherever he may live, will bid you welcome.

The President replied as follows:

Dr. Noble Wiley Jones: As President of this college I desire that you convey to the President and Fellows of the American College of Physicians the grateful thanks of the Fellows and members of this college for their message of goodwill and their appreciation of its significance to the English-speaking people on the shores of the Pacific Ocean.

The Royal Australasian College of Surgeons.

Sir Hugh Devine, as representative of the Royal Australasian College of Surgeons, delivered the message from that college, as follows:

We, the President and Council of the Royal Australasian College of Surgeons, send this message of greeting and goodwill to the Royal Australasian College of Physicians on the occasion of its foundation.

This welcome to our medical brethren is made even more cordial by the belief that our two colleges, working together in a spirit of unity and concord, will ever strive not only to promote the knowledge and to foster the ideals of our profession throughout and beyond the confines of Australia and New Zealand, but also, in concert with our more ancient sister colleges in Britain, to strengthen the bonds which unite our countries to the British Empire.

We beg the President and Council of the Royal Australasian College of Physicians to accept, with this address, the gift of a council table as a token of our best wishes for the future progress of their college.

The President replied as follows:

Sir Hugh Devine: As President of this college I desire that you will convey to the President and Fellows of your college the thanks of the Fellows and members of this college, not only for the present cordial greetings and valuable gift of a table, but also for the great help and sympathy this college has always received from the Royal Australasian College of Surgeons.

The Royal College of Physicians and Surgeons of Canada.

The following message was received from the Royal College of Physicians and Surgeons of Canada. Owing to accidental delays in transmission this message arrived too late to be read at the inaugural ceremony.

> On behalf of the President, Council and Fellows of the Royal College of Physicians and Surgeons of Canada, may I ask you to convey to the Royal Australasian College of Physicians our thanks for your very kind invitation, and our very best wishes for the success of your college. We hope that in the future we may send delegates to your annual meetings and that your college will be able to reciprocate.
>
> With very kind greetings from the President and Council of our college,
>
> I am,
>
> Yours sincerely,
>
> WARREN S. LYMAN, M.D.,
>
> Honorary Secretary.

Medicine, Past and Present.

The Censor-in-Chief then asked the permission of the President to call upon Dr. Herbert Morley Fletcher to deliver his address entitled "Medicine, Past and Present". This address will be published in a later issue of this journal.

Honorary Fellowship of the Royal Australasian College of Physicians.

The Censor-in-Chief presented Dr. Morley Fletcher to the President in the following terms:

> Mr. President: By resolution of the Council and by virtue of the authority committed to me as Censor-in-Chief, I present to you for admission as an Honorary Fellow of the Royal Australasian College of Physicians Herbert Morley Fletcher, Master of Arts and Doctor of Medicine of the University of Cambridge, Doctor of Laws of the University of Belfast, Fellow of the Royal College of Physicians of London. Dr. Fletcher is consulting physician to Saint Bartholomew's Hospital; he is a member of the Council of the Royal College of Physicians of London and was formerly its senior censor. Dr. Fletcher has played a most important part in the teaching of medicine in Great Britain and has exerted a beneficial influence of the highest order over its practice. Not only because of his eminence in the science and art of medicine, but also because he comes to us as the representative of that venerable institution from which so many of the ideals of our newly founded college are derived and to which we already owe much, your Council deems it most fitting that Dr. Herbert Morley Fletcher should be the first Honorary Fellow of the Royal Australasian College of Physicians.

Dr. Fletcher was then robed by the Censor-in-Chief as a fellow of the Royal Australasian College of Physicians and admitted by the President to Honorary Fellowship of the college. Dr. Fletcher briefly acknowledged his appreciation of this honour.

The Censor-in-Chief then presented Dr. Noble Wiley Jones to the President in the following terms:

> Mr. President: By resolution of the Council and in virtue of the authority committed to me as Censor-in-Chief, I now present to you for admission as an Honorary Fellow of the Royal Australasian College of Physicians Noble Wiley Jones, of Oregon, in the United States of America, Bachelor of Arts of Leland Stamford University, Doctor of Medicine of the University of Chicago, Fellow of the American College of Physicians and one of its Vice-Presidents, professor of Clinical Medicine in the University of Oregon. He is one of the foremost exponents of the practice of medicine in his own great country. In token not only of his personal distinction but also in grateful recognition of the debt which medicine owes to the work of physicians in the United States of America, your Council feels that it is peculiarly appropriate that the name of Dr. Noble Wiley Jones should be second on the Roll of Honorary Fellows of the Royal Australasian College of Physicians.

Dr. Jones was then robed by the Censor-in-Chief as a Fellow of the Royal Australasian College of Physicians and admitted by the President to Honorary Fellowship of the college. Dr. Jones briefly acknowledged his appreciation of this honour.

Finale.

After the playing of the National Anthem the procession was again formed of councillors and office-bearers of the college, the representatives of other colleges, the Chancellor and Deputy Chancellor of the University of Sydney, the President, His Excellency's Aides-de-camp and His Excellency the Governor. The procession left the hall by the eastern door.

EXAMINATION FOR MEMBERSHIP.

The written examination for the membership of the Royal Australasian College of Physicians will be held in capital cities of Australia where candidates are offering, on Saturday, February 25, 1939. The clinical examination will be held at Melbourne on March 21 and 22, 1939.

It is necessary that application forms should be in the hands of the Honorary Secretary, 185, Macquarie Street, Sydney, not later than January 28, 1939.

There will also be a clinical examination at Sydney about the end of August, 1939, and the corresponding written

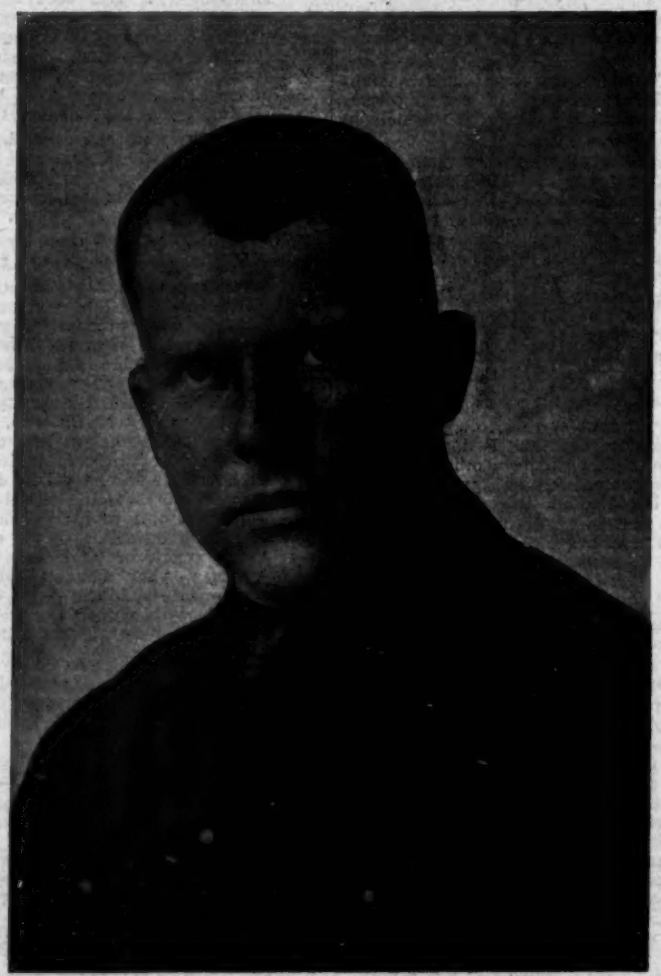
examinations will be held in the capital cities about one month previous to this. Applications for this examination should reach the Honorary Secretary not later than June 30, 1939.

The above dates are subject to minor alterations.

Obituary.

HARRIE CARISFORT EDMOND DONOVAN.

HARRIE CARISFORT EDMOND DONOVAN, who died on September 10, 1938, was the son of William Christopher Donovan, a bank manager. He was born at Paddington, New South Wales, in July, 1882. He received his early education at the Sydney Grammar School, then went on to the University of Sydney. He obtained the degree of Bachelor of Medicine in 1906. He was a Fellow of the Royal Australasian College of Surgeons and a Fellow of the College of Obstetricians and Gynæcologists.



After graduation he held an appointment on the resident medical staff of Saint Vincent's Hospital, Sydney, for a period, then commenced general practice at Ballina, New South Wales. Later he conducted a general practice at Waverley, Sydney. For a number of years prior to his death he practised at Macquarie Street, Sydney, as an obstetrician and gynæcologist.

He was an honorary assistant physician on the staff of Saint Vincent's Hospital, Sydney, from 1910 to 1919, and for many years prior to his death he was an honorary obstetrician and gynæcologist to The Women's Hospital, Crown Street, Sydney. It is by his association with the Women's Hospital that he will be best remembered by medical practitioners in New South Wales. The members of the honorary staff of the hospital will cherish memories of a loyal colleague; those whom he met as students or resident medical officers will remember his kindness and forbearance and his ability as a teacher.

Little need be said of Donovan's professional knowledge and skill. He had profited from his very wide experience, and he was expert alike in midwifery and in gynæcological surgery. In the management of women in labour or attention to the sick he was firm, gentle and patient.

Donovan served with the Australian Army Medical Corps during the Great War, attaining the rank of Major. For a time he was adjutant to the Ninth Field Ambulance in France; later he was transferred on account of illness to Horseferry Road, and eventually he was invalided home.

He always took a keen interest in sport, and attained some prowess himself. In his early years he acquired considerable skill as a gymnast, and won the championship of the Sydney Grammar School.

He had two sons and a daughter. One son, Dr. Kevin Cormack Donovan, practises his profession at Gladstone, Queensland.

Donovan was cheerful, courageous and generous—indeed a lovable man. He will be greatly missed by his colleagues and his patients.

The sympathy of the medical profession is extended to Mrs. Donovan and her family in their bereavement.

Dr. E. Ludowici writes:

I knew the late Harrie Carisfort Edmond Dovonan as a colleague at The Women's Hospital for many years, and he acted for me during many abscences from my private practice.

He was a man to whom one could trust one's patients with the feeling that they would be fully satisfied, and yet not lose their faith in their own medical attendant. Keen, cheerful, active-minded and capable, he was the ideal of a practitioner who as obstetric surgeon had to be both a surgeon and physician. His training as a general practitioner fitted him admirably for the responsible work of a hospital honorary.

As lecturer to students in clinical obstetrics and also to the nurses, he was interesting and methodical, displaying the efficiency which comes from full knowledge.

During the last few years, though suffering from an illness which partially crippled him, and which without doubt had its origin during service in the Great War, he displayed an amazing fortitude in the face of great difficulties, continuing with his hospital as well as with his private work almost to the end.

Never was there a more loyal and trusty colleague, and he is sadly missed.

Dr. T. Dixon Hughes writes:

Harrie Carisfort Edmond Donovan was a great man, if honesty, sincerity and *æquanimitas* are traits of the great. If we add to these the possession of a cheerful courage that surmounted all difficulties, we can appreciate a man who just walked out of his practice to serve his country, and, like Kipling's idea of a man, came back to build it up afresh. He delighted in the search for truth, and this led him to the forefront of his specialty. No illogical methods of reasoning could withstand the light of his discerning criticism.

It has been my privilege to be associated with the late Harrie Donovan for the past thirteen years as a member of the staff of The Women's Hospital, Crown

Street, with which he was associated for many years. Throughout his term of office he was a friend and a counsellor to all.

Harrie Donovan was a man who wrote his testimonials in four lines, and so we may epitomize his life: he was a seeker after truth, and, above all, he was a gentleman.

JAMES COOK.

WE regret to announce the death of Dr. James Cook, which occurred on December 19, 1938, at Geelong, Victoria.

KEITH MOORE WHITING.

WE regret to announce the death of Dr. Keith Moore Whiting, which occurred on December 21, 1938, at Parramatta, New South Wales.

ARCHIBALD BROWN CAMPBELL.

WE regret to announce the death of Dr. Archibald Brown Campbell, which occurred on December 19, 1938, at Ballarat, Victoria.

Correspondence.

THE FIRST FIFTY-TWO NAMES IN THE MEDICAL REGISTER OF SOUTH AUSTRALIA.

SIR: In my article entitled as above (October 29, 1938, page 732) I have given the total number of medical men registered in South Australia up to November, 1919, as 1,023. This is taken from an official list published by the Medical Board in 1930. The highest registered number in this list is 1018. The difference is explained as follows, and at the same time I am pointing out several printer's errors, for example: Numbers 1012, 1014, 1015 and 1017 are given with an extra hundred, 1112 *et cetera*. Six numbers have *A* or *B* appended to them. Robinson, R. A. McW., should be number 567, not 567*B* (there is no other number 567). Walpole, G. A., is number 364. Goerger, O., number 254 (there is another number 254), appears again after number 364 for additional registration, and Gosse, C., is number 364*B*. Mead, C. S., is number 480; Hayward, G. C., number 480*A*; Lane, C. S., number 480*B*, and Nall, J. F., number 480*C* (not 480*A* as in the list). Souter, J. C., is number 485 and Drummond, J. H. G., is 485*B* (there is no number 485*A*). These add five to the 1,018.

In Mr. Sholl's letter in your issue of November 26, 1938, page 926, he takes exception to the spelling of his grandfather's name (number 52 in the list) as Scholl. The name William Horatio Scholl is number 52 in the Medical Register and the name is spent Scholl also in the minutes. However, in the *Government Gazette* of 1849, his name was correctly spelt and he was gazetted as William Horatio Sholl. Having always known the name of his son, the Under-Secretary, to be spelt Sholl, I had the records in the Medical Register specially looked up again to see what the spelling was. It seems quite clear that the spelling of Scholl was due to a clerical mistake. As a matter of fact, in my manuscript the Under-Secretary's name was spent correctly (Sholl), but this was changed, probably by the proof-reader, to Scholl to conform with the Register spelling.

The reason why 52 names were chosen was that this number completed those registered up to 1849.

Yours, etc.,

The University of Adelaide, J. B. CLELAND.
December 15, 1938.

ACCIDENTAL HÆMORRHAGE.

SIR: I have read with great interest Dr. Drummond's excellent results in accidental hæmorrhage, and I have been greatly surprised at Dr. Callagher's criticism of certain parts of his treatment. Surely Dr. Callagher would not be so radical in his treatment as to have recommended the performance of Cæsarean section in the early stages in all of the cases reported in Dr. Drummond's series. We must all agree that for good results in obstetrics conservatism is coming more and more to the front, and this is particularly so in the treatment of accidental hæmorrhage both here and abroad, where the older method of Cæsarean section is being replaced by the more conservative method of treating the all-important symptom of shock. When this is done it is found that delivery by the vaginal route is possible in many cases of severe accidental hæmorrhage. As in surgery so in obstetrics, the same rule applies that to give the patient the best chance of surviving we have to treat the shock, and only when it is passed off or relieved can we think of radical procedures, and fortunately in practice when the shock is treated, in most of these severe cases, we are greatly relieved to find we can deliver our patient by the vaginal route without resorting to drastic surgical methods which would have been carried out had we not favoured primary conservative treatment.

Yours, etc.,

Leith House, ROLAND NATTRASS.
220, St. George's Terrace,
Perth, Western Australia.
December 19, 1938.

NOTICE.

A MEMBER of the New South Wales Medical Board has informed us that during recent months a number of medical graduates of foreign universities have been referred to him by medical practitioners in the hope that he might use his influence to provide employment for them. He points out: first, that this is embarrassing to him; secondly, that the board has to administer the Act as it stands; thirdly, that the board has no positions to offer, and, fourthly, that it is unfair of a man to approach an individual member of a body, such as a medical board, with the object of obtaining a privilege either for himself or someone in whom he is interested. The proper procedure in such cases is for the foreign graduate to interview the Secretary of the Medical Board and not members of the Board.

Books Received.

MINOR MEDICAL OPERATIONS FOR SENIOR MEDICAL STUDENTS AND RECENTLY QUALIFIED PRACTITIONERS, by K. Harris, M.A., M.D., F.R.C.P., and E. Harris, M.B., B.S., D.P.H.; 1938. London: H. K. Lewis and Company Limited. Crown 8vo, pp. 210, with 41 illustrations. Price: 7s. 6d. net.

ALCOHOL AND HUMAN LIFE, by C. C. Weeks, M.R.C.S., L.R.C.P., with a foreword by T. Barlow, F.R.C.P., M.D., F.R.S.; Second Edition, revised and enlarged; 1938. London: H. K. Lewis and Company Limited. Crown 8vo, pp. 464, with 20 illustrations. Price: 6s. net.

RESEARCH MONOGRAPHS OF THE AMERICAN ORTHOPSYCHIATRIC ASSOCIATION. No. 3: A VISUAL MOTOR GESTALT TEST AND ITS CLINICAL USE, by L. Bender, M.A., M.D.; 1938. New York: American Orthopsychiatric Association. Crown 4to, pp. 186, with illustrations.

EVERYDAY SURGERY, by L. Rogers, M.Sc., F.R.C.S., F.R.C.S.E., F.R.A.C.S., F.A.C.S., and A. L. d'Abreu, M.B., Ch.M., F.R.C.S., with an introduction by G. Grey Turner, D.Ch., M.S., F.R.C.S., F.R.A.C.S., F.A.C.S.; 1938. London: Edward Arnold and Company. Demy 8vo, pp. 292, with illustrations Price: 12s 6d. net.

THE ABNORMAL IN OBSTETRICS, by C. Berkeley, M.A., M.C., M.D., F.R.C.P., F.R.C.S., M.M.S.A., F.C.O.G.; V. Bonney, M.S., M.D., B.Sc., F.R.C.S., F.R.A.C.S., M.R.C.P., and D. MacLeod, M.S., M.B., F.R.C.S., F.R.C.P., M.C.O.G.; 1938. London: Edward Arnold and Company Limited. Demy 8vo, pp. 533. Price: 18s. net.

SCHAFER'S ESSENTIALS OF HISTOLOGY, DESCRIPTIVE AND PRACTICAL, FOR THE USE OF STUDENTS, edited by H. M. Carleton, M.A., B.Sc., D.Phil.; Fourteenth Edition; 1938. London: Longmans, Green and Company. Medium 8vo, pp. 630, with illustrations. Price: 16s. net.

THE OCCIPITO-POSTERIOR POSITION: ITS MECHANISM AND TREATMENT, WITH A NEW CONCEPTION OF THE ROLE OF THE PELVIC FLOOR, by R. Beard, M.C., M.B., B.S., F.R.C.S., F.R.A.C.S., F.C.O.G.; Second Edition; 1938. Adelaide: F. W. Preece and Sons. Demy 8vo, pp. 39, with illustrations.

SHORT-WAVE THERAPY: THE MEDICAL USES OF ELECTRICAL HIGH FREQUENCIES, by E. Schliephake; authorized English translation by R. K. Brown, B.A., M.D., D.P.H., from the third German edition, with a foreword by E. P. Cumberbatch, M.A., M.B., B.Ch., F.R.C.P., D.M.R.E.; Second English Edition; 1938. London: The Actinic Press Limited. Medium 8vo, pp. 296, with illustrations. Price: 21s. net.

VITAMINS AND VITAMIN DEFICIENCIES, by L. J. Harris, Ph.D., Sc.D., D.Sc., F.I.C.; Volume I: Introductory and Historical, Vitamin B_1 and Beri-Beri, with a foreword by F. G. Hopkins, O.M., F.R.C.P., F.R.S.; 1938. London: J. and A. Churchill Limited. Large crown 8vo, pp. 218, with 50 illustrations. Price: 8s. 6d. net.

REPORT ON CARDIAZOL TREATMENT AND ON THE PRESENT APPLICATION OF HYPOGLYCÆMIC SHOCK TREATMENT IN SCHIZOPHRENIA, by W. R. Thomas, M.D., F.R.C.P., D.P.M., and I. G. H. Wilson, M.D., M.R.C.P., D.P.M.; 1938. London: His Majesty's Stationery Office. Medium 8vo, pp. 70. Price: 1s. net.

BACKGROUND TO MODERN SCIENCE: TEN LECTURES AT CAMBRIDGE ARRANGED BY THE HISTORY OF SCIENCE COMMITTEE, 1936, by F. M. Cornford, W. Dampier, Lord Rutherford, W. L. Bragg, F. W. Aston, A. S. Eddington, J. A. Ryle, G. H. F. Nuttall, R. C. Punnett, J. B. S. Haldane, edited by J. Needham and W. Pagel; 1938. Cambridge: The University Press. Crown 8vo, pp. 255. Price: 7s. 6d. net.

THE ESSENTIALS OF MODERN SURGERY, edited by R. M. Handfield-Jones, M.C., M.S., F.R.C.S., and A. E. Porritt, M.A., M.Ch., F.R.C.S.; 1938. Edinburgh: E. and S. Livingstone. Medium 8vo, pp. 1141, with 501 illustrations. Price: 30s. net.

Diary for the Month.

JAN. 3.—New South Wales Branch, B.M.A.: Executive and Finance Committee.
JAN. 10.—New South Wales Branch, B.M.A.: Council (Quarterly).
JAN. 12.—South Australian Branch, B.M.A.: Council.
JAN. 13.—Queensland Branch, B.M.A.: Council.
JAN. 25.—Victorian Branch, B.M.A.: Council.
JAN. 27.—Queensland Branch, B.M.A.: Council.
FEB. 1.—Victorian Branch, B.M.A.: Branch.
FEB. 1.—Western Australian Branch: Council.
FEB. 2.—South Australian Branch, B.M.A.: Council.
FEB. 3.—Queensland Branch, B.M.A.: Branch.
FEB. 7.—New South Wales Branch, B.M.A.: Organization and Science Committee.
FEB. 10.—Queensland Branch, B.M.A.: Council.
FEB. 14.—New South Wales Branch, B.M.A.: Executive and Finance Committee.
FEB. 21.—New South Wales Branch, B.M.A.: Ethics Committee.
FEB. 22.—Victorian Branch, B.M.A.: Council.
FEB. 23.—South Australian Branch, B.M.A.: Branch.
FEB. 24.—Queensland Branch, B.M.A.: Council.
FEB. 28.—New South Wales Branch, B.M.A.: Medical Politics Committee.

Medical Appointments Vacant, etc.

For announcements of medical appointments vacant, assistants, *locum tenentes* sought, etc., see "Advertiser", pages xiv to xvii.

CHILDREN'S HOSPITAL (INCORPORATED), PERTH, WESTERN AUSTRALIA: Junior Resident Medical Officers.

DEVON PUBLIC HOSPITAL, LATROBE, TASMANIA: House Surgeon.

INFECTIOUS DISEASES HOSPITAL, FAIRFIELD, VICTORIA: Resident Medical Officers.

SCHOOL OF PUBLIC HEALTH AND TROPICAL MEDICINE, SYDNEY, NEW SOUTH WALES: Diploma in Tropical Medicine and Diploma in Public Health.

VICTORIAN EYE AND EAR HOSPITAL, MELBOURNE, VICTORIA: Resident Medical Superintendent.

WESTERN AUSTRALIAN PUBLIC SERVICE: Junior Medical Officers.

Medical Appointments: Important Notice.

MEDICAL PRACTITIONERS are requested not to apply for any appointment referred to in the following table without having first communicated with the Honorary Secretary of the Branch named in the first column, or with the Medical Secretary of the British Medical Association, Tavistock Square, London, W.C.1.

BRANCHES.	APPOINTMENTS.
NEW SOUTH WALES: Honorary Secretary, 135, Macquarie Street, Sydney.	Australian Natives' Association. Ashfield and District United Friendly Societies' Dispensary. Balmain United Friendly Societies' Dispensary. Leichhardt and Petersham United Friendly Societies' Dispensary. Manchester Unity Medical and Dispensing Institute, Oxford Street, Sydney. North Sydney Friendly Societies' Dispensary Limited. People's Prudential Assurance Company Limited. Phœnix Mutual Provident Society.
VICTORIAN: Honorary Secretary, Medical Society Hall, East Melbourne.	All Institutes or Medical Dispensaries. Australian Prudential Association, Proprietary, Limited. Mutual National Provident Club. National Provident Association. Hospital or other appointments outside Victoria.
QUEENSLAND: Honorary Secretary, B.M.A. House, 225, Wickham Terrace, Brisbane, B.17.	Brisbane Associate Friendly Societies' Medical Institute. Proserpine District Hospital. Members accepting LODGE appointments and those desiring to accept appointments to any COUNTRY HOSPITAL are advised, in their own interests, to submit a copy of their Agreement to the Council before signing.
SOUTH AUSTRALIAN: Secretary, 178, North Terrace, Adelaide.	All Lodge appointments in South Australia. All contract Practice Appointments in South Australia.
WESTERN AUSTRALIAN: Honorary Secretary, 205, Saint George's Terrace, Perth.	All Contract Practice Appointments in Western Australia.

Editorial Notices.

MANUSCRIPTS forwarded to the office of this journal cannot under any circumstances be returned. Original articles forwarded for publication are understood to be offered to THE MEDICAL JOURNAL OF AUSTRALIA alone, unless the contrary be stated.

All communications should be addressed to the Editor, THE MEDICAL JOURNAL OF AUSTRALIA, The Printing House, Seamer Street, Glebe, New South Wales. (Telephones: MW 2651-2.)

Members and subscribers are requested to notify the Manager, THE MEDICAL JOURNAL OF AUSTRALIA, Seamer Street, Glebe, New South Wales, without delay, of any irregularity in the delivery of this journal. The management cannot accept any responsibility or recognise any claim arising out of non-receipt of journals unless such a notification is received within one month.

SUBSCRIPTION RATES.—Medical students and others not receiving THE MEDICAL JOURNAL OF AUSTRALIA in virtue of membership of the Branches of the British Medical Association in the Commonwealth can become subscribers to the journal by applying to the Manager or through the usual agents and booksellers. Subscriptions can commence at the beginning of any quarter and are renewable on December 31. The rates are £3 for Australia and £2 5s. abroad *per annum* payable in advance.

JUL 26 1939

Registered at the G.P.O., Sydney, for Transmission by Post as a Newspaper. Published Weekly. Price 1s.

Medical Library

THE MEDICAL JOURNAL OF AUSTRALIA

VOL. II.—25TH YEAR. SYDNEY, SATURDAY, DECEMBER 31, 1938. No. 27.

COMMONWEALTH OF AUSTRALIA
Department of Health

Commonwealth "INSULIN"

Insulin is available at the following prices:

5 c.c. phial of 100 units (20 units per c.c.)	1/6
5 c.c. phial of 200 units (40 units per c.c.)	2/10
5 c.c. phial of 300 units (60 units per c.c.)	4/3

Every batch of Commonwealth Insulin is carefully tested before issue and the UNIT EMPLOYED IS THAT OF THE STANDARD ISSUED UNDER THE AUTHORITY OF THE LEAGUE OF NATIONS.

COMMONWEALTH INSULIN IS — HIGHLY PURIFIED, STABLE, ACTIVE, STERILE.

Commonwealth PITUITARY EXTRACT

IS PHYSIOLOGICALLY STANDARDIZED IN ACCORDANCE WITH THE RECOMMENDATIONS OF THE LEAGUE OF NATIONS TECHNICAL CONFERENCE.

1 box of 6 × 1 c.c. Surgical,	20 International Units per c.c.	8/6
1 box of 6 × ½ c.c. Surgical,	20 International Units per c.c.	5/-
1 box of 6 × 1 c.c. Obstetrical,	10 International Units per c.c.	5/-
1 box of 6 × ½ c.c. Obstetrical,	10 International Units per c.c.	3/6

Supplies may be obtained from the Commonwealth Serum Laboratories, Parkville, Victoria, and also from the following: Director-General of Health, Canberra; Chief Quarantine Officer (General), Anzac Square, Adelaide Street, Brisbane, Qld.; Chief Quarantine Officer (General), Customs House, Circular Quay, Sydney, N.S.W.; Chief Quarantine Officer (General), C.M.L. Building, 41-47 King William Street, Adelaide, S.A.; Chief Quarantine Officer (General), G.P.O., Perth, W.A.; Chief Quarantine Officer (General), Commonwealth Health Laboratory, Launceston, Tasmania.

COMMONWEALTH SERUM LABORAOTRIES
PARKVILLE, N.2 — VICTORIA — AUSTRALIA

BAILLIÈRE
Tindall and Cox

BOOKS OF IMPORTANCE

TROPICAL NUTRITION AND DIETETICS
By LUCIUS B. NICHOLLS, M.D. Pp. 164.
Price 7s. 6d.

AIDS TO BACTERIOLOGY
By W. PARTRIDGE, F.I.C., and H. W. SCOTT WILSON, B.Sc., B.Ch. *Sixth Edition.* Pp. vii + 300. **Price 5s.**

TEXTBOOK OF NEURO-RADIOLOGY
By CECIL P. G. WAKELEY, D.Sc., F.R.C.S., and ALEXANDER ORLEY, M.D., D.M.R.E. Pp. 336, 229 Illustrations. **Price 25s.**

AIDS TO EMBRYOLOGY
By R. H. HUNTER. *Third Edition.* Pp. viii + 178. **Price 3s. 6d.**

THE FOOT
By NORMAN C. LAKE, M.D., M.S., F.R.C.S. *Second Edition.* Pp. viii + 366. **Price 12s. 6d.**

AIDS TO BIOCHEMISTRY
By E. A. COOPER, D.Sc., F.I.C., and D. NICHOLAS, B.A., A.I.C. *Second Edition.* Pp. viii + 214. **Price 4s. 6d.**

ROSE AND CARLESS' SURGERY
By CECIL P. G. WAKELEY and J. B. HUNTER. 2 Vols. 1,720 pages, with 953 Illustrations. **Price 30s.**

CIVILIZATION AND DISEASE
By C. P. DONNISON, M.D., M.R.C.P. Pp. xvi + 222. **Price 10s. 6d.**

AIDS TO HISTOLOGY
By ALEX. GOODALL, M.D., F.R.C.P. *Fourth Edition.* Pp. viii + 152. **Price 3s. 6d.**

PAPERS ON PSYCHO-ANALYSIS
By ERNEST JONES, M.D., M.R.C.P. *Fourth Edition.* Pp. x + 643. **Price 25s.**

TEXTBOOK OF MENTAL DEFICIENCY
By A. F. TREDGOLD, M.D., F.R.C.P. Pp. xvi + 556, with 33 Plates. **Price 25s.**

AIDS TO ZOOLOGY
By H. LISTER, M.D., F.Z.S. *Second Edition.* Pp. viii + 260. **Price 4s. 6d.**

DISEASES OF THE SKIN
Revised by R. M. B. MACKENNA, M.D., M.R.C.P. Pp. xvi + 558, with 46 Coloured Plates and 168 Figures. **Price 20s.**

OCCUPATIONAL TREATMENT OF MENTAL ILLNESS
By J. I. RUSSELL, M.B., Ch.B., F.R.F.P.S., D.P.M. Pp. xvi + 232, with 41 Illustrations. **Price 6s.**

AIDS TO PHYSIOLOGY
By H. DRYERRE, Ph.D., M.R.C.S., L.R.C.P., F.R.S.E. *Second Edition.* Pp. viii + 196, with 63 Figures. **Price 3s. 6d.**

MODERN DIETARY TREATMENT
By M. ABRAHAMS, M.A., M.Sc., and E. M. WIDDOWSON, B.Sc., Ph.D. Pp. x + 328. **Price 8s. 6d.**

AIDS TO PATHOLOGY
By H. CAMPBELL, M.D., F.R.C.S., and K. CAMPBELL, M.B., F.R.C.S. *Seventh Edition.* Pp. viii + 264, with 12 Figures. **Price 4s. 6d.**

SURGERY OF SYMPATHETIC NERVOUS SYSTEM
By PROF. G. E. GASK, F.R.C.S., and PROF. J. PATERSON ROSS, M.S., F.R.C.S. Pp. xii + 186, with 49 Illustrations. **Price 16s.**

AIDS TO THE TREATMENT OF DISEASES OF CHILDREN
By F. M. B. ACCEW, M.D., M.R.C.P. Pp. vii + 330. **Price 4s. 6d.**

OPHTHALMIC OPERATIONS
By H. GRIMSDALE, M.B., F.R.C.S., and E. BREWERTON, F.R.C.S. Pp. x + 322, with 105 Illustrations. **Price 17s. 6d.**

7 AND 8, HENRIETTA STREET, LONDON, W.C.2

ARCHIBALD OLLÉ
MASSEUR
Member A.M.A. et A.T.N.A.
Dry Hot Air, Static, Electric Light, Diathermy, and High Frequency Currents.
32 CHARLOTTE STREET, ASHFIELD.
Telephone: UA 1171.

PERCIVAL D. OLLÉ
M.S.R., B.P.A., N.R. (Eng.),
MASSEUR,
PHYSIO-THERAPEUTIST.
Ultra Short and Short Wave Diathermy. Ultra Violet (Mercury Vapour). Infra-Red, Electrical Iontophoresis. And all modern treatments used in Physical Medicine.
"Wembury",
42 ELIZABETH ST., ASHFIELD.
Telephone UA 1097.

CHIROPODY
T. R. CHRISTIE
Diploma Scientific Chiropody.
Master Chiropodist.
Room 19, Fourth Floor,
Challis House,
10 Martin Place, Sydney.

MICROSCOPES.

Research, Students' and other models, by W. & H. Seibert (Germany), Leitz (Germany), Rosenbaum (Germany), C. Baker (London), new and S.H., from £11/10/-. Other models, 5/6 to £100.
Also Diagnostic Sets, Ophthalmoscopes, Stethoscopes, Microscope Accessories, Stains, Reagents, Mounted Slides, Telescopes, Binoculars, Natural History Books, new and second hand.
OIL IMMERSIONS by leading makers from £3/10/-. *Catalogues free.*
N. H. SEWARD PTY. LTD.
"Optical House," 457 Bourke St., Melbourne, C.1.

Australasian Massage Association
(Victorian Branch)
LIST OF MEMBERS MAY BE OBTAINED FROM THE SECRETARY
All members trained at the University and Public Hospital
MISS E. CAMPBELL,
61 Collins Street, Melbourne
Central 3070.

Surgical Instrument Cases
The Austral Jewel Case Co. wishes to advise the Medical Profession that they are manufacturers of cases to hold Surgical Instruments. Cases can be made to order, to hold any number of instruments, fitted correctly, so that there is no danger of the instruments being damaged.
QUOTES ON APPLICATION.
York House, 294 Little Collins Street, Melbourne.
P.O. Box 1626 M. Tel. Cen. 6985.

1938
LIST OF MEMBERS
of the branches of
THE BRITISH MEDICAL ASSOCIATION
IN AUSTRALIA
NOW AVAILABLE
OBTAINABLE FROM
AUSTRALASIAN MEDICAL PUBLISHING COMPANY, LIMITED
THE PRINTING HOUSE - - - - - - - SEAMER STREET, GLEBE

The Modern Aid to the Obstetrician

The Williams Obstetric Bedstead

Illustrated above is this famous bedstead. It is the most up-to-date Labour Bedstead manufactured.

AMONG ITS MANY FEATURES ARE:

ADJUSTABLE LIMB SUPPORT FOR LEFT LATERAL POSITION.
CAPABLE OF BEING DIVIDED INTO TWO SECTIONS.
FITTED WITH STANDARD AND PULLEY FOR HANGING OF WEIGHTS.
THE U-LIFT PERMITS ELEVATION OF FRAME FOR SHOCK CASES.
MOBILITY.
LIFT OUT HEAD RAIL.

OBTAINABLE ONLY FROM THE PATENTEES AND MANUFACTURERS.

Acme Bedstead Co. Pty. Ltd.

McEVOY STREET, ALEXANDRIA, SYDNEY

Telephones: M 4206, M 4207.

● No Maternity Hospital is efficiently equipped without them. 'Phone or write for fuller particulars.

Wholly set up, printed and published at The Printing House, Seamer Street, Glebe, Sydney, N.S.W., by ARTHUR FREDERICK ROOTS SIMPSON, of Fairholm Street, Strathfield, New South Wales, on behalf of the AUSTRALASIAN MEDICAL PUBLISHING COMPANY, LIMITED, Seamer Street, Glebe, Sydney, New South Wales.